

The use of sentinel species in health disparities research



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Siberian Yupik people of St. Lawrence Island, Alaska



Qawalangin
Tribe of Unalaska

Yuma



Mayan people of Lake
Atitlán, Guatemala



Anindilyakwa people of Groote Eylandt, Australia



community based participatory research (CBPR)

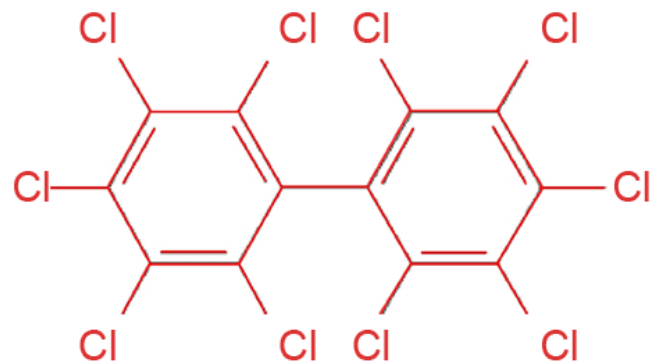
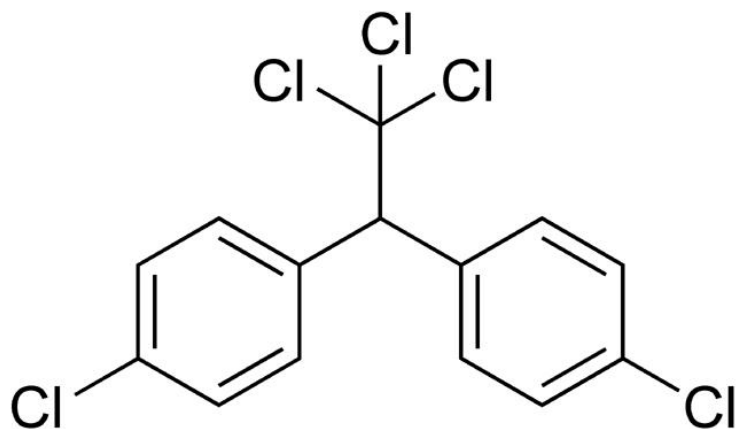
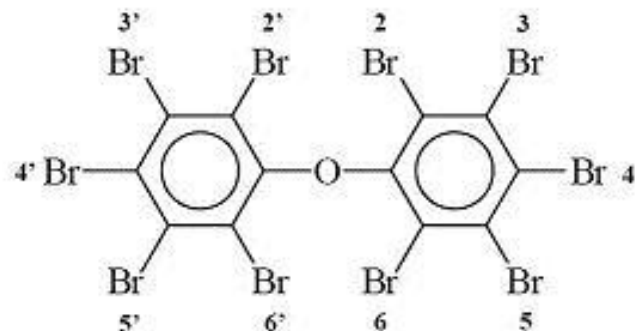
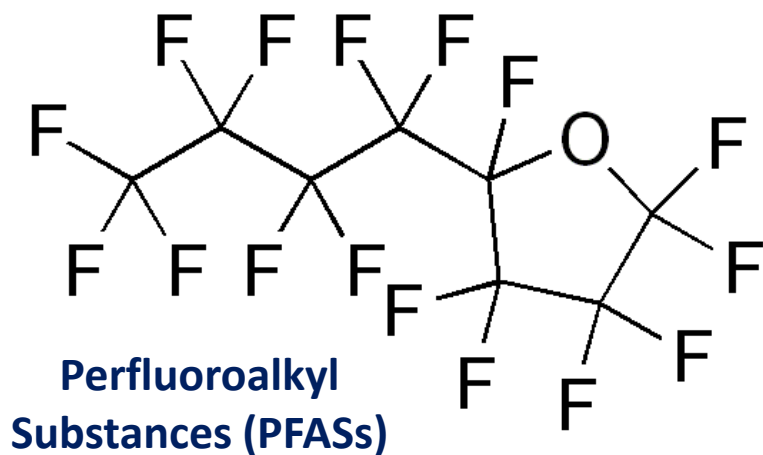
Siberian Yupik people of St. Lawrence Island, Alaska



Anindilyakwa people of Groote Eylandt, Australia



Persistent Organic Pollutants



Contaminated Sites

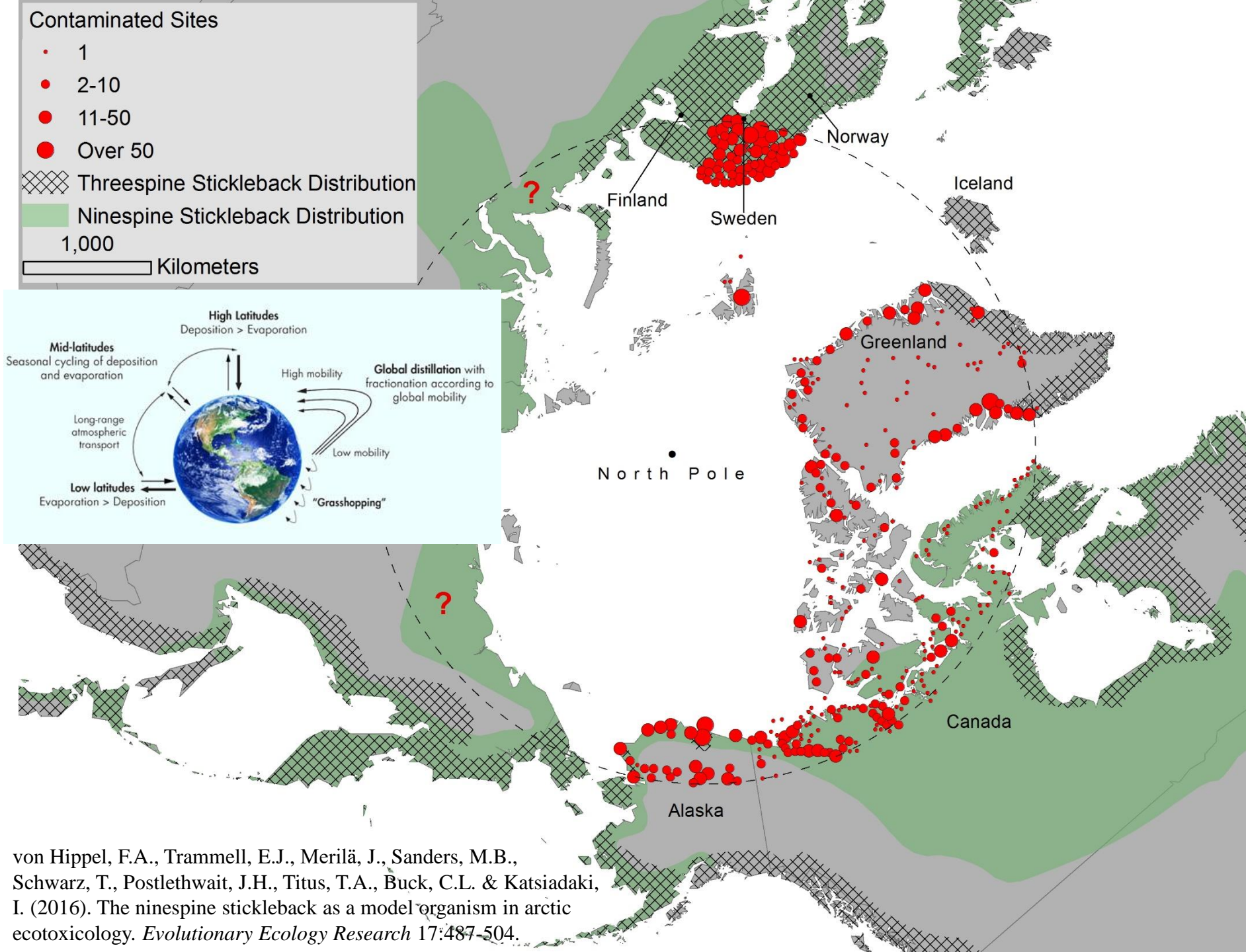
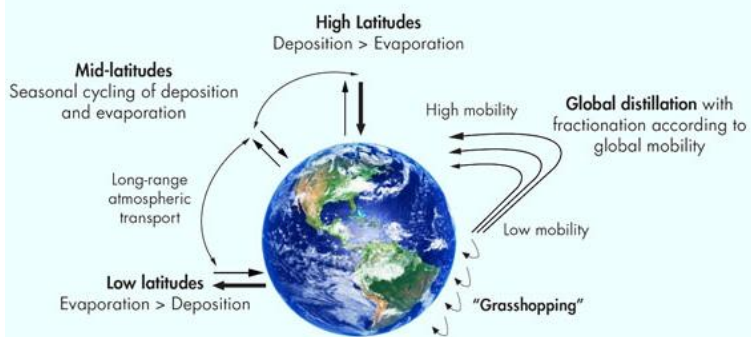
- 1
- 2-10
- 11-50
- Over 50

Threespine Stickleback Distribution

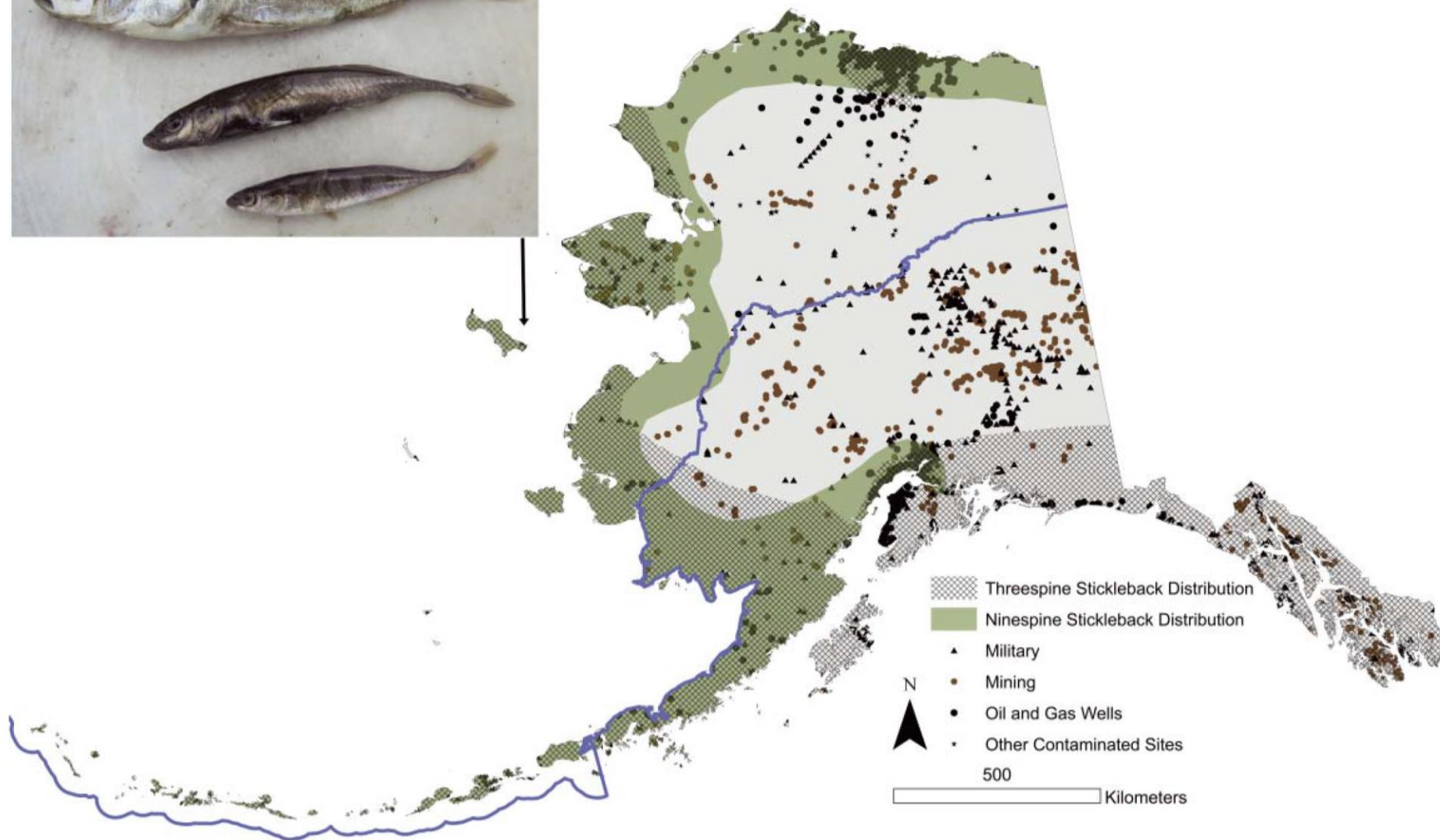
Ninespine Stickleback Distribution

1,000

Kilometers



von Hippel, F.A., Trammell, E.J., Merilä, J., Sanders, M.B., Schwarz, T., Postlethwait, J.H., Titus, T.A., Buck, C.L. & Katsiadaki, I. (2016). The ninespine stickleback as a model organism in arctic ecotoxicology. *Evolutionary Ecology Research* 17:487-504.



Threespine Stickleback Distribution

Ninespine Stickleback Distribution

▲ Military

● Mining

● Oil and Gas Wells

■ Other Contaminated Sites

500



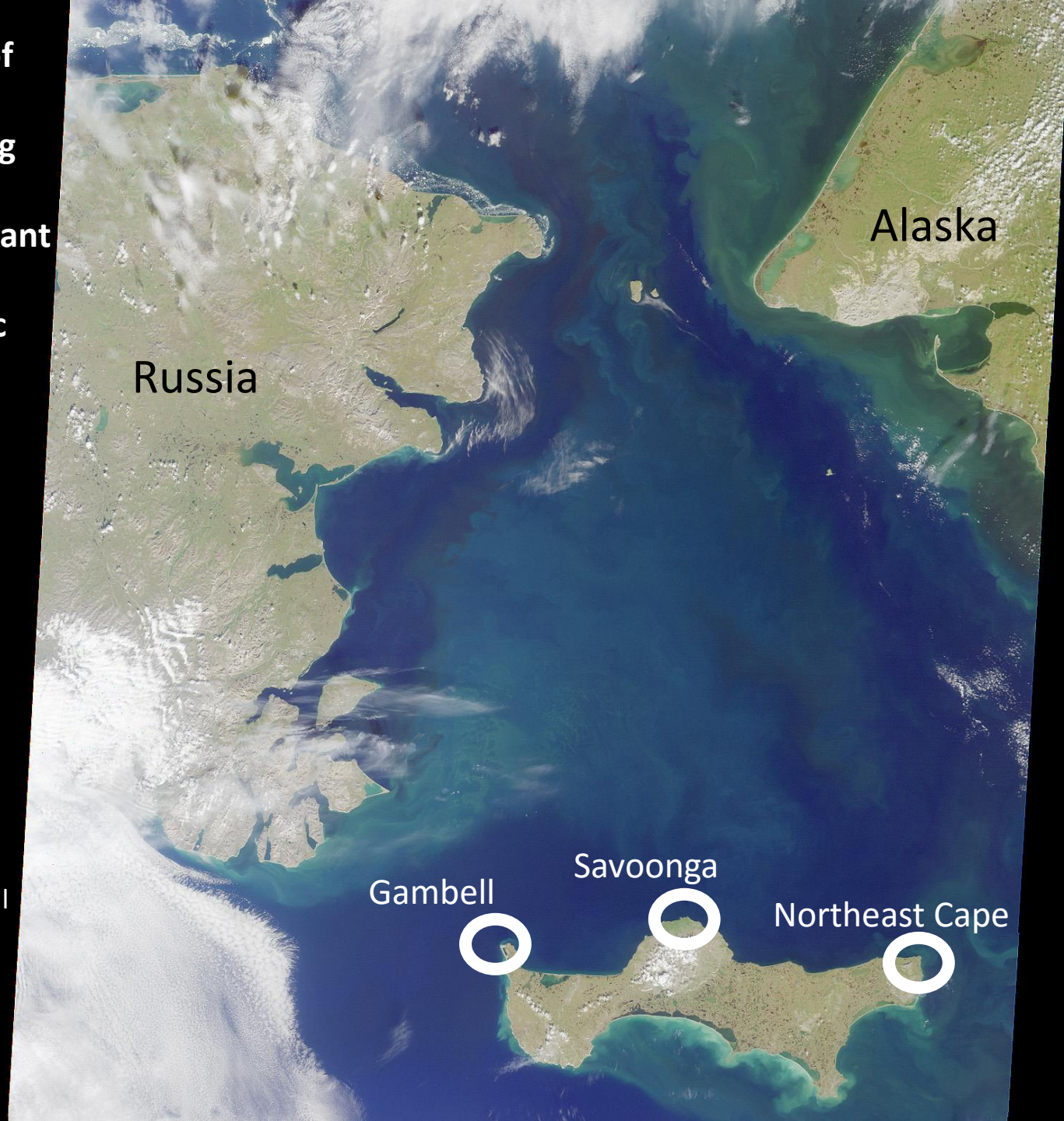
Kilometers

Health Patterns of Concern

- **Cancers**
- **Thyroid disease**
- **Diabetes**
- **Heart disease**
- **Birth defects, low birthweight babies, premature births, stillbirths, miscarriages**
- **Other reproductive health problems**



**“Protecting the Health of
Future Generations:
Assessing and Preventing
Exposures to Endocrine-
Disrupting Flame Retardant
Chemicals & PCBs in
Two Alaska Native Arctic
Communities on
St. Lawrence Island”**



National Institute of Environmental
Health Sciences RO1, 2011-2016
Miller, P.K., von Hippel, F.A., Buck,
C.L. & Carpenter, D.
NIEHS 1RO1ES019620 &
2RO1ES019620

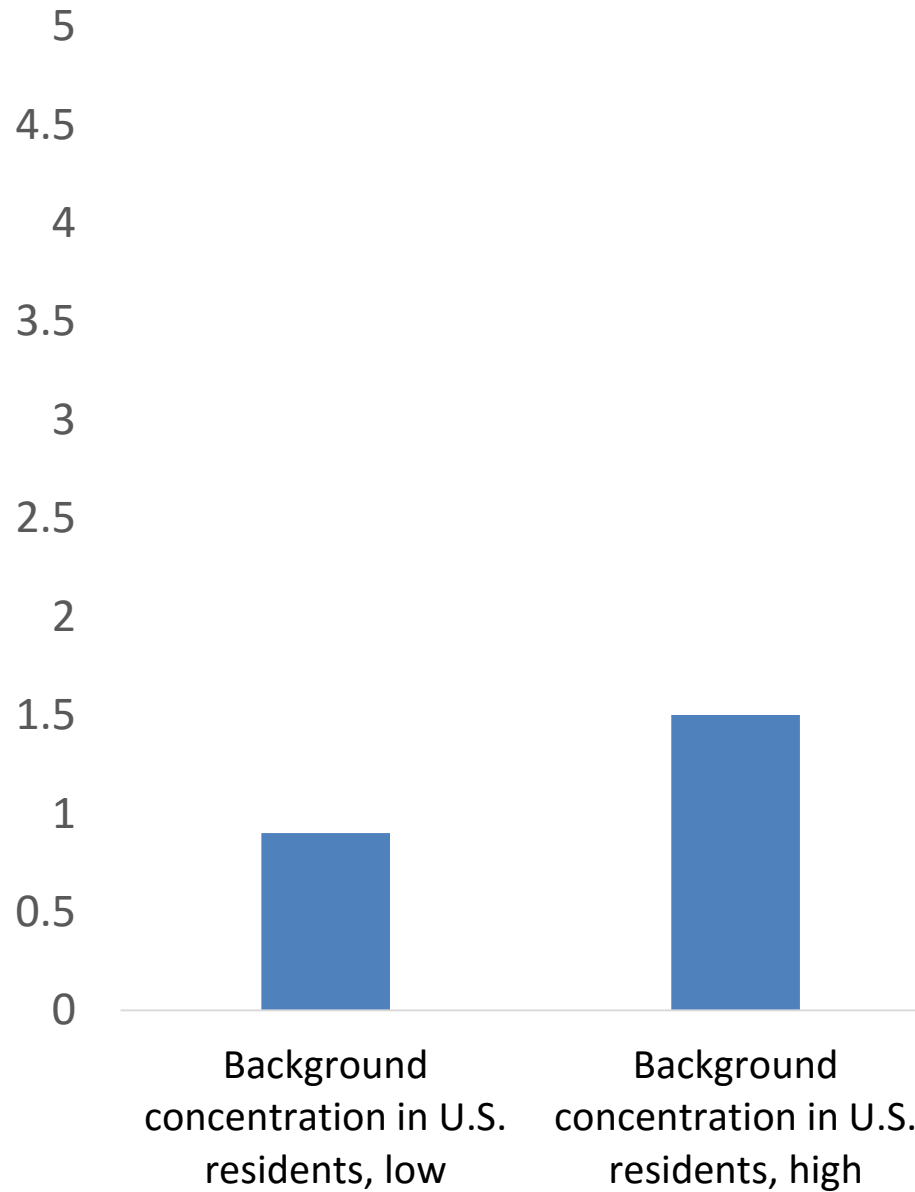


Community outreach: Pam Miller & ACAT
Ecotoxicology: Frank von Hippel
Endocrinology: Loren Buck
Human health research: David Carpenter
Gene expression: John Postlethwait

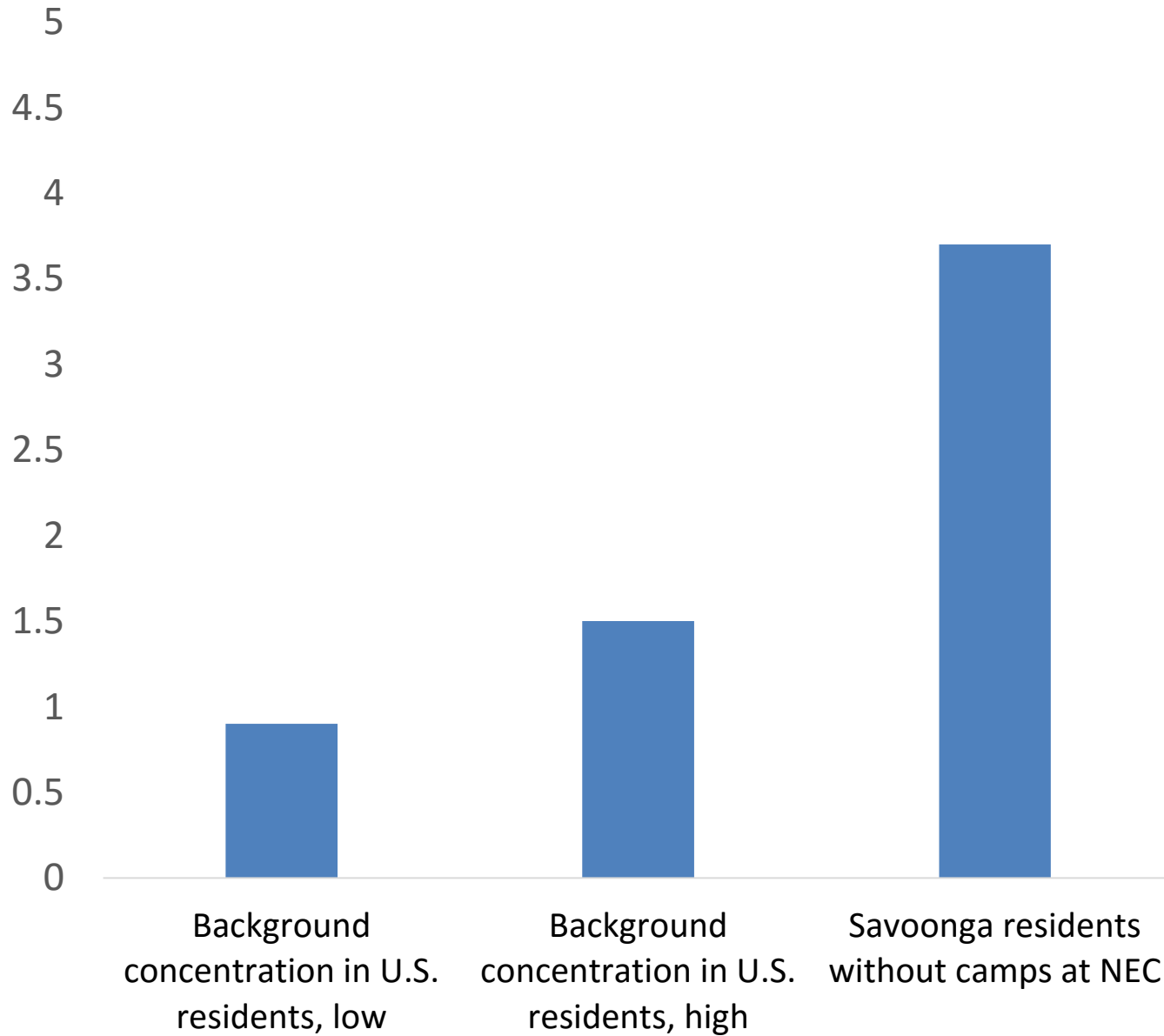
**PCBs in blood serum of
St. Lawrence Island people**



Mean [PCB] (ppb, wet weight)

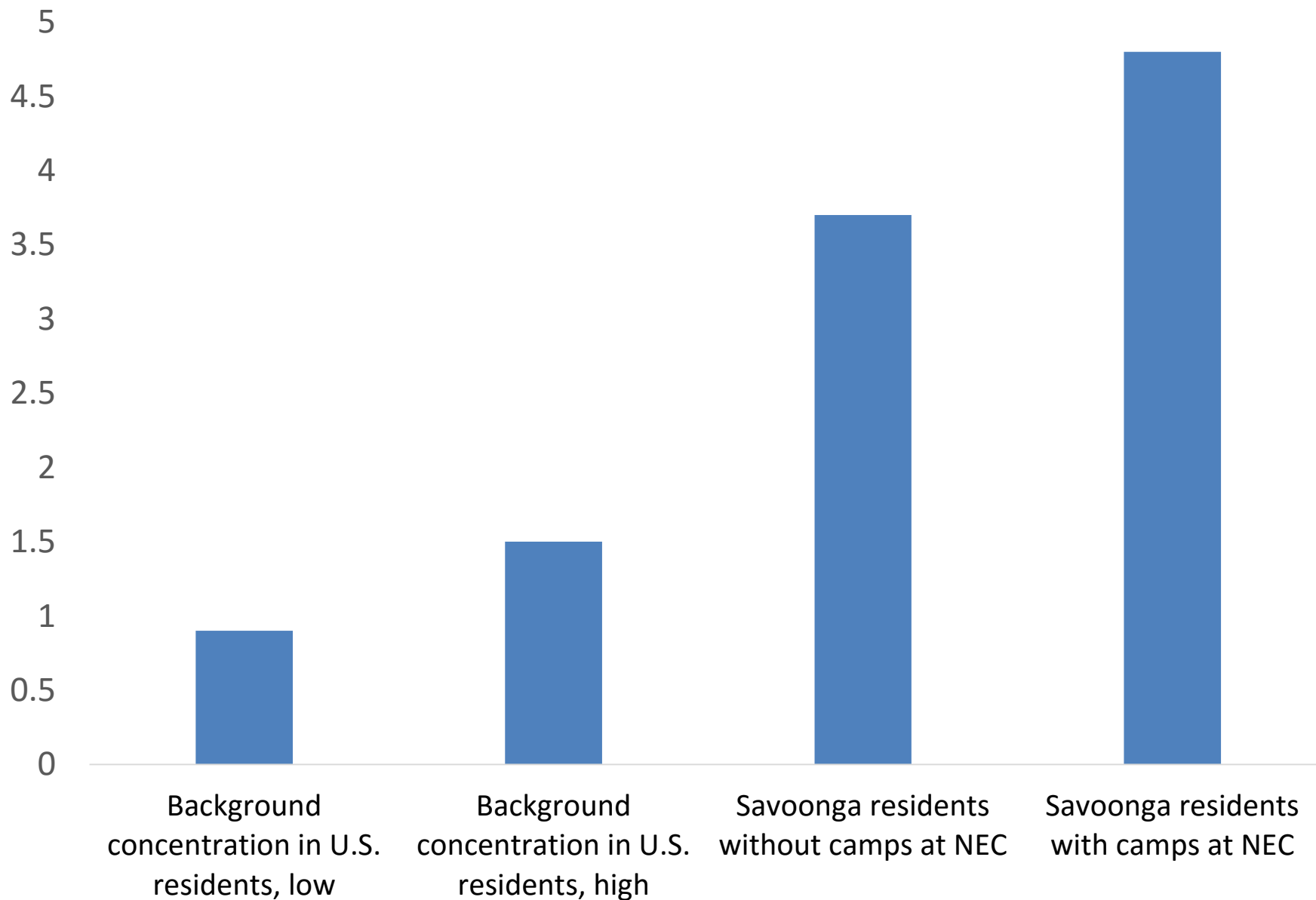


Mean [PCB] (ppb, wet weight)



data from Carpenter & Miller (2011)

Mean [PCB] (ppb, wet weight)



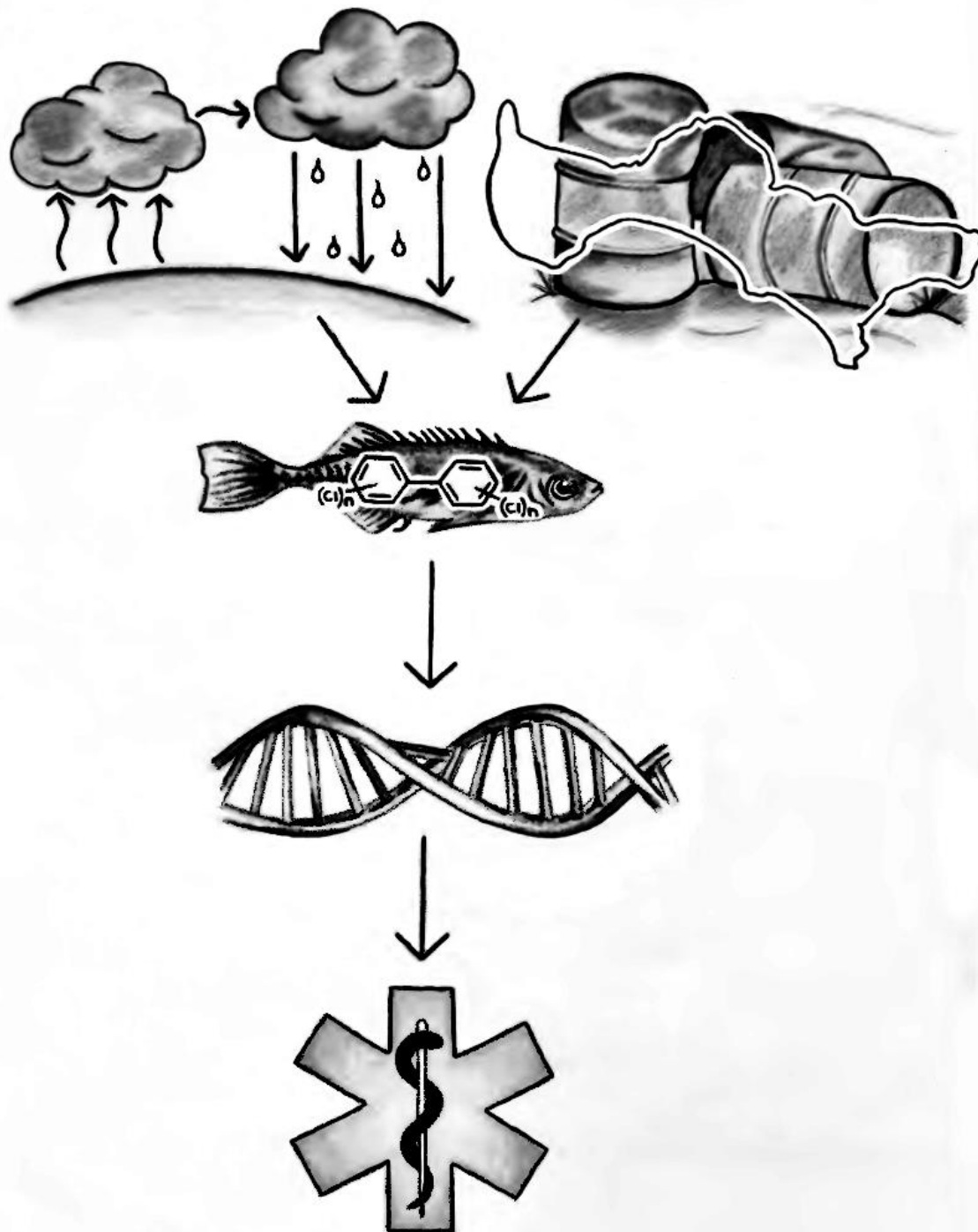
data from Carpenter & Miller (2011)

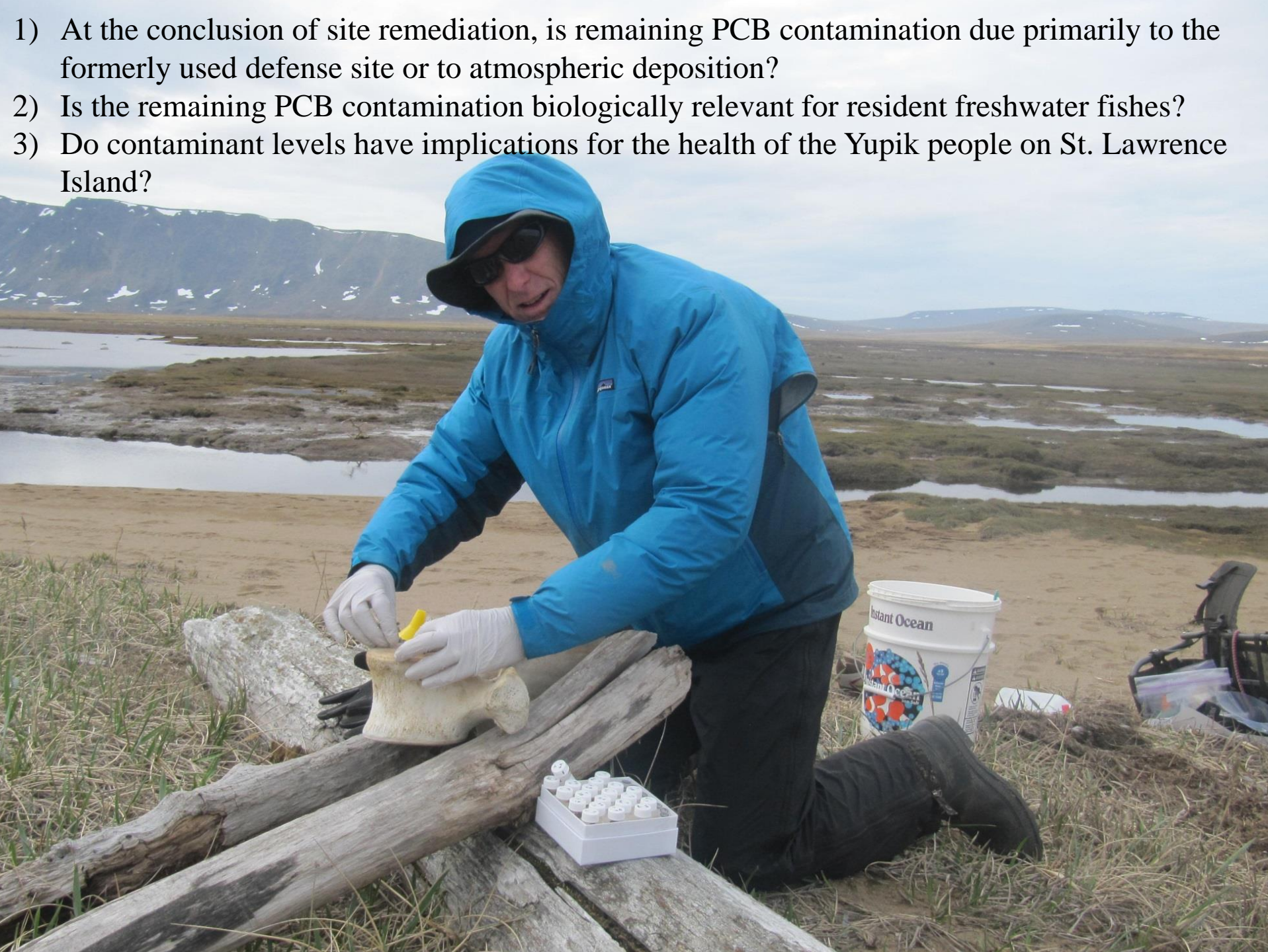
White Alice Communication Site, operational 1957-1972

Above ground structures & debris removed in 2003

\$123 million spent on site remediation

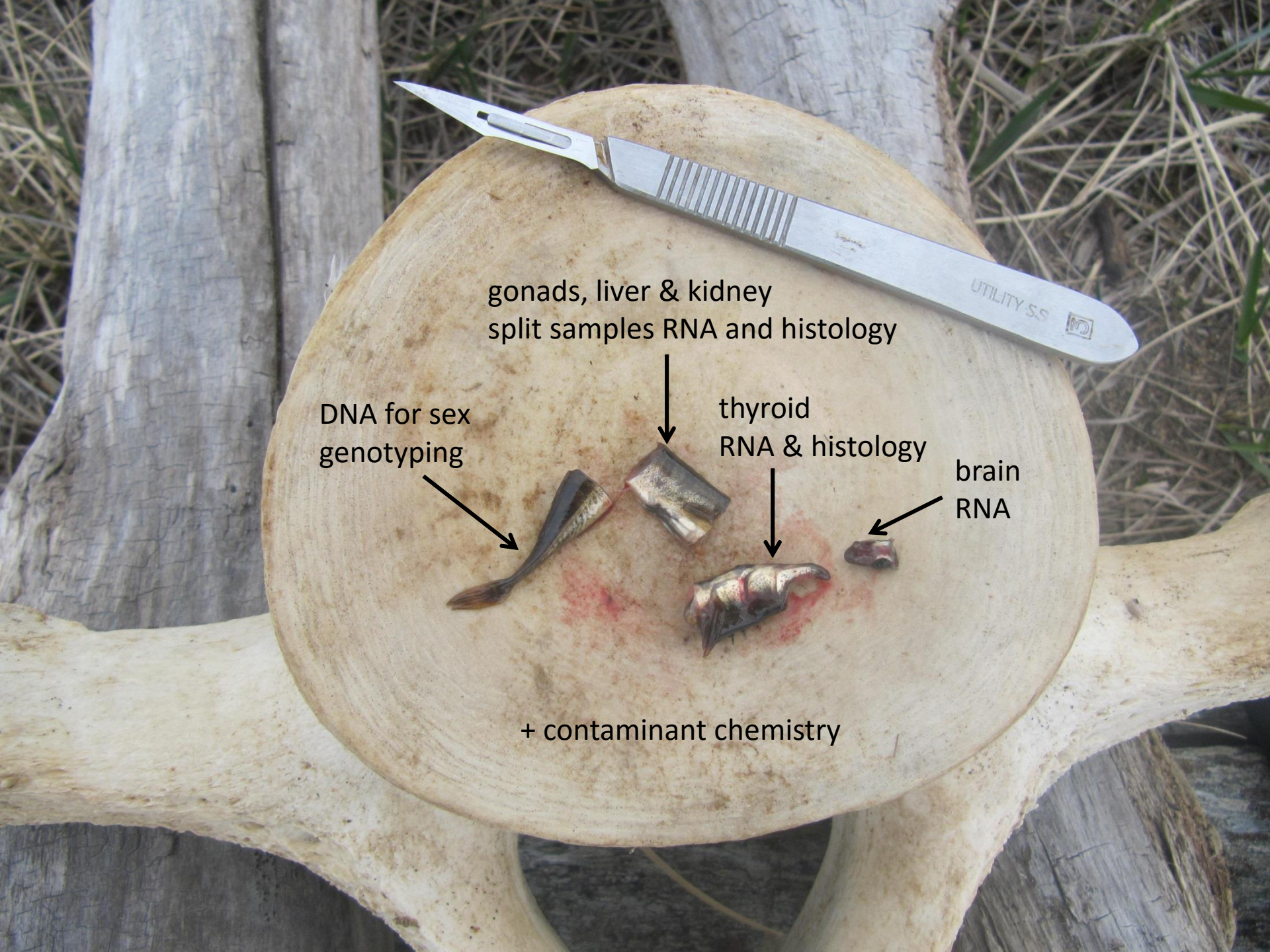






- 1) At the conclusion of site remediation, is remaining PCB contamination due primarily to the formerly used defense site or to atmospheric deposition?
- 2) Is the remaining PCB contamination biologically relevant for resident freshwater fishes?
- 3) Do contaminant levels have implications for the health of the Yupik people on St. Lawrence Island?





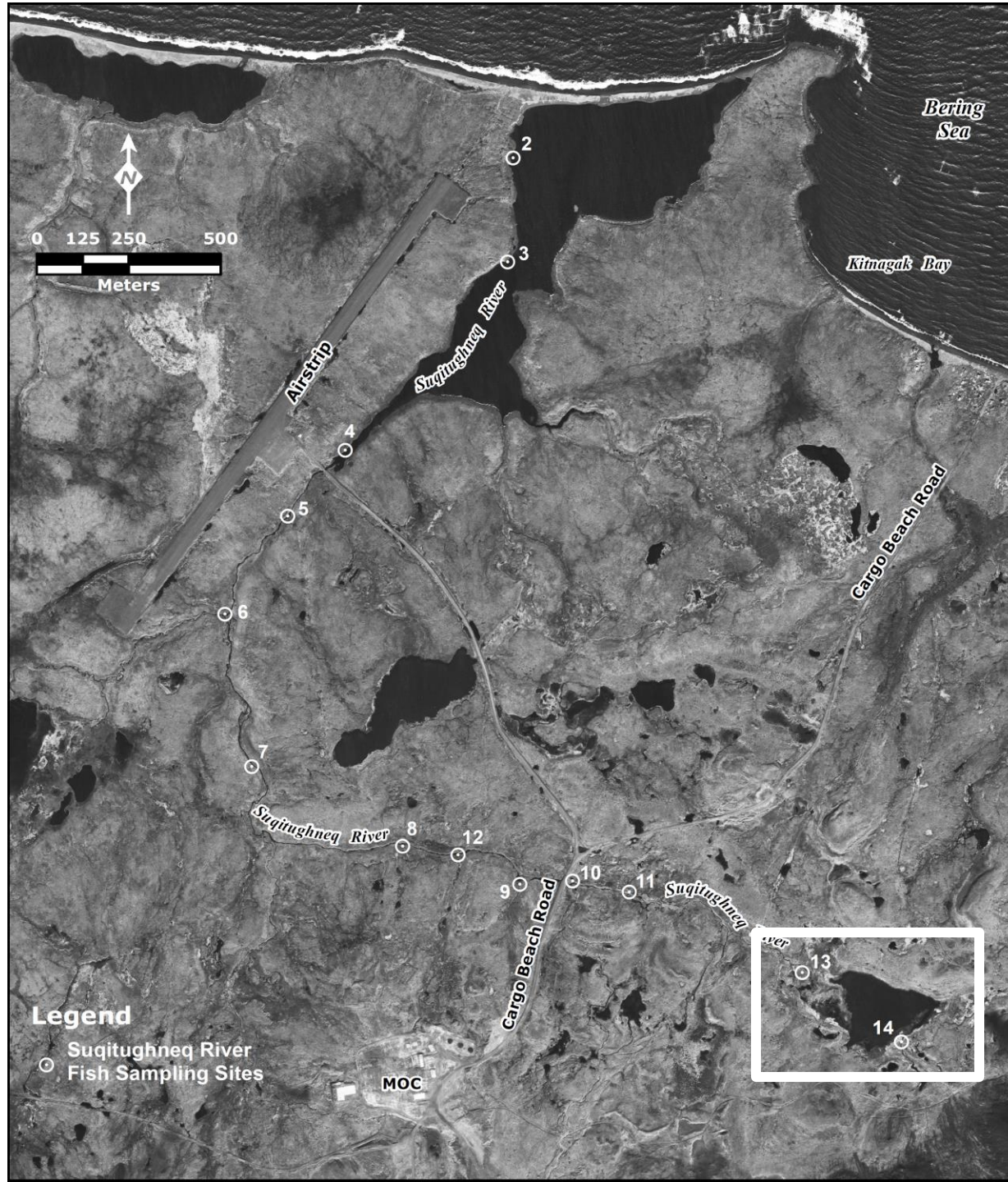
gonads, liver & kidney
split samples RNA and histology

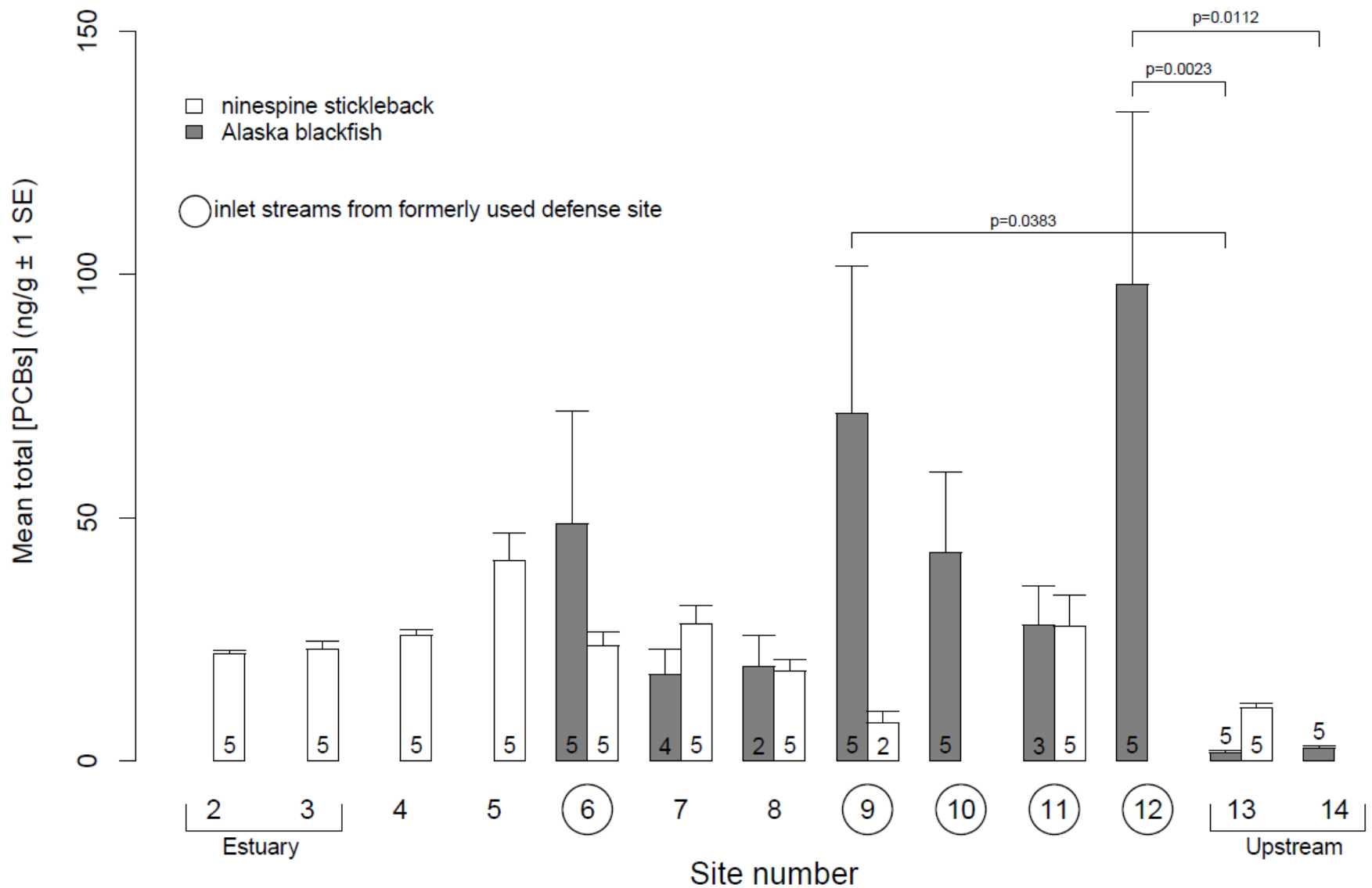
DNA for sex
genotyping

thyroid
RNA & histology

brain
RNA

+ contaminant chemistry



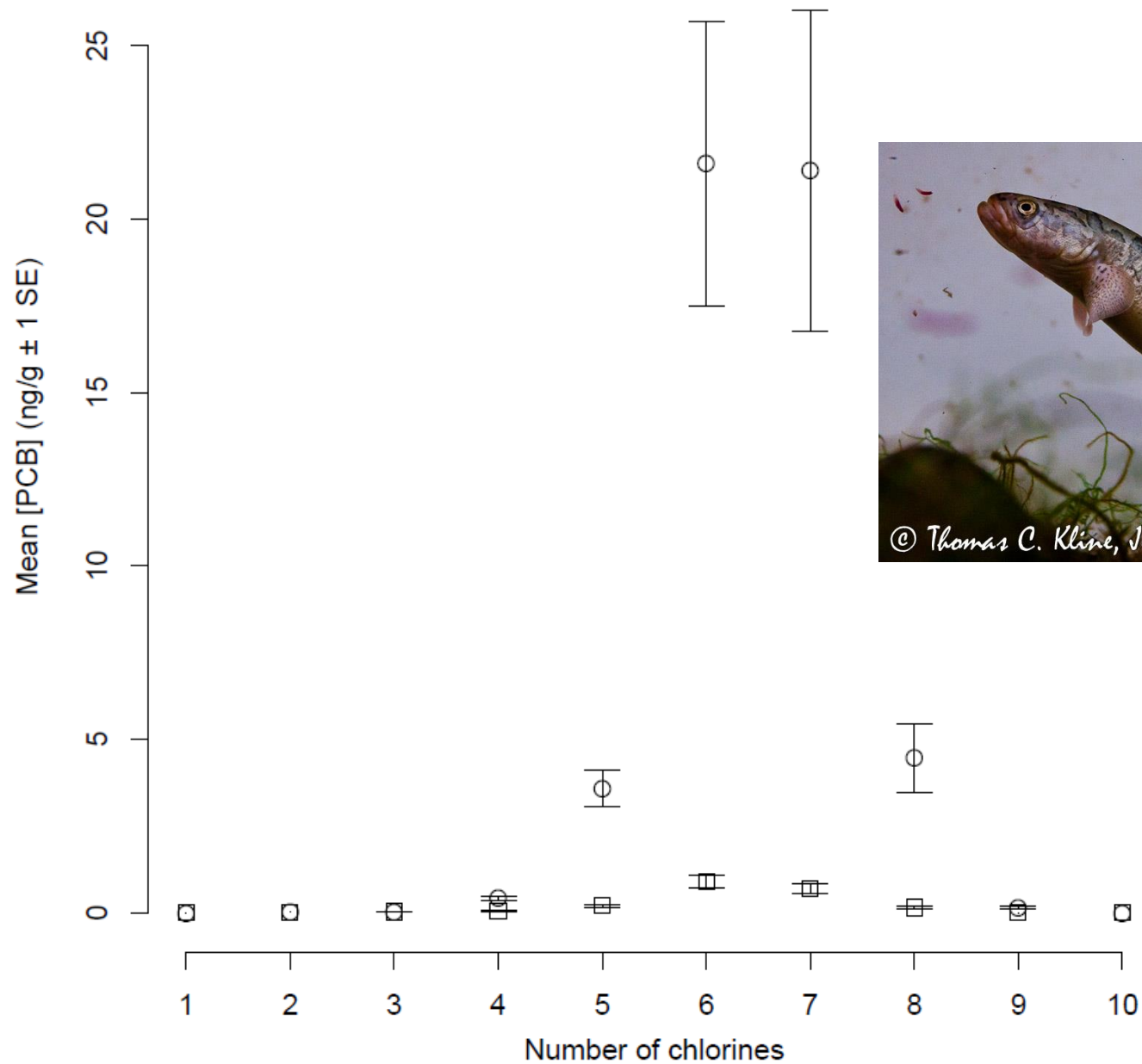


von Hippel, F.A., Miller, P.K., Carpenter, D.O., Dillon, D., Smayda, L., Katsiadaki, I., Titus, T.A., Batzel, P., Postlethwait, J.H. & Buck, C.L. (2018). Endocrine disruption and differential gene expression in sentinel fish on St. Lawrence Island, Alaska: health implications for indigenous residents. *Environmental Pollution* 234:279-287.

B) Alaska blackfish

○ Downstream; n=29

□ Upstream; n=10

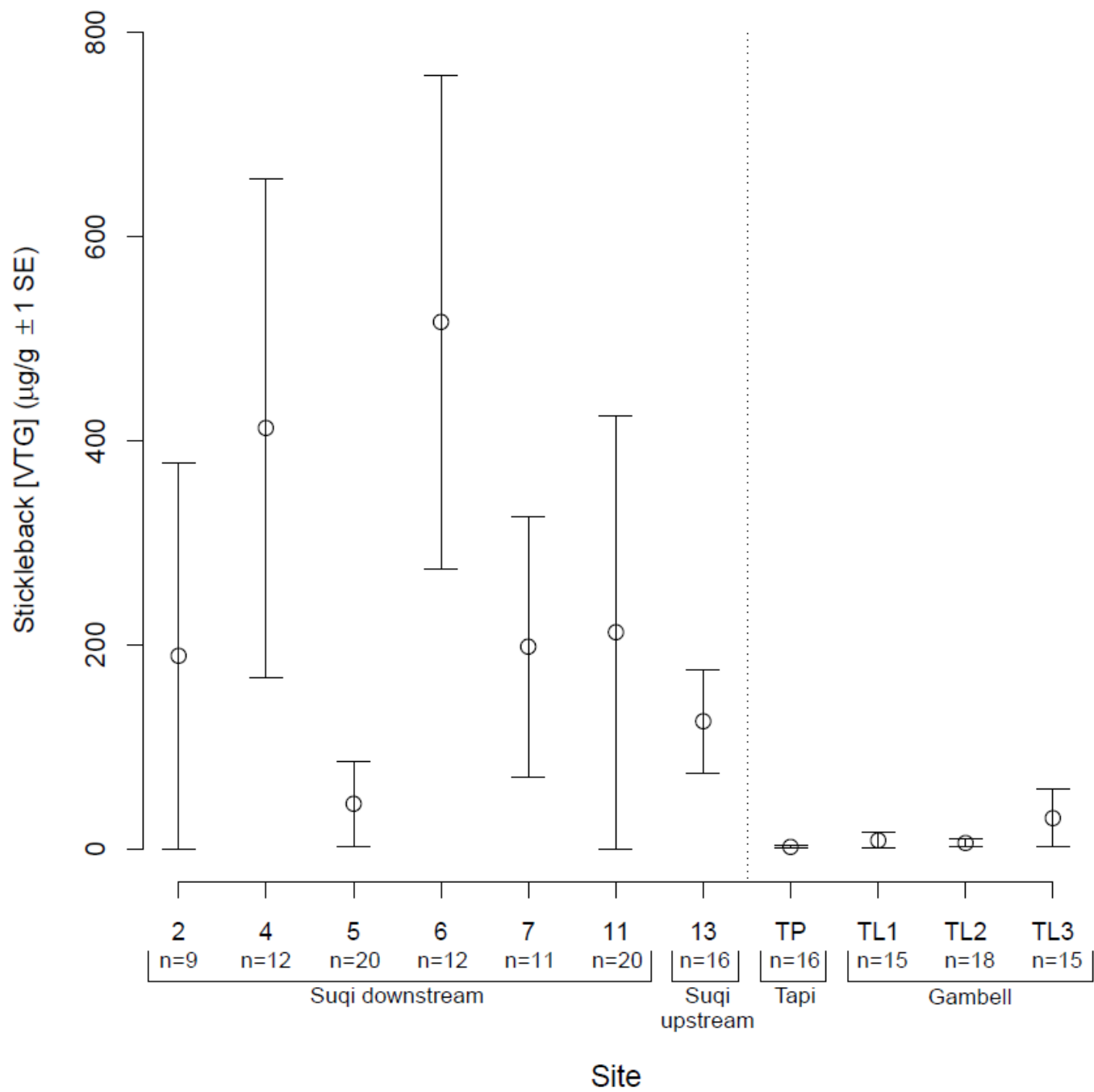


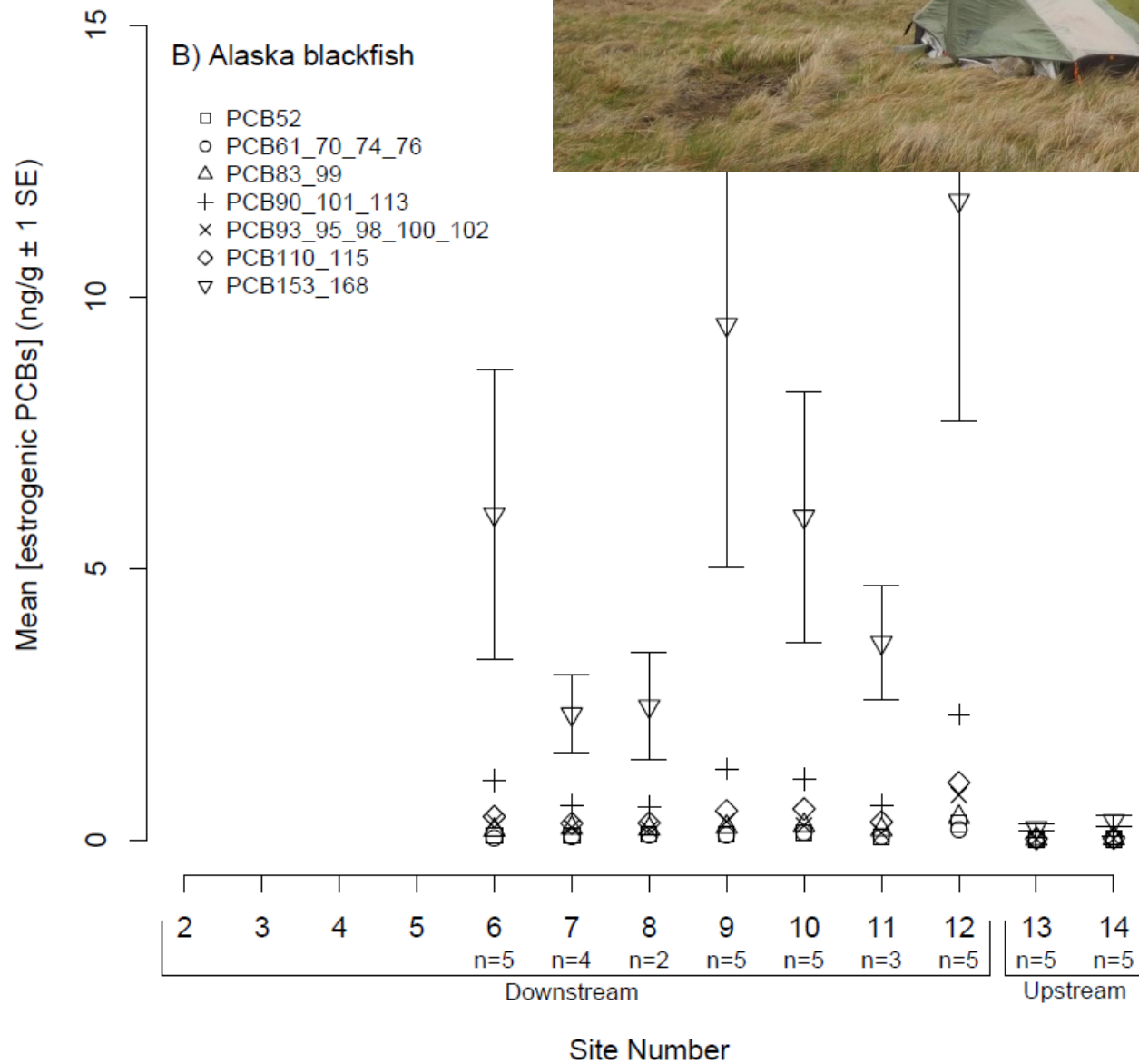
Levels of PCBs in the fish are still high,
even though clean-up is considered complete...
and contaminant chemistry reveals a mostly local source (FUDS),
but are these [PCB] biologically meaningful?

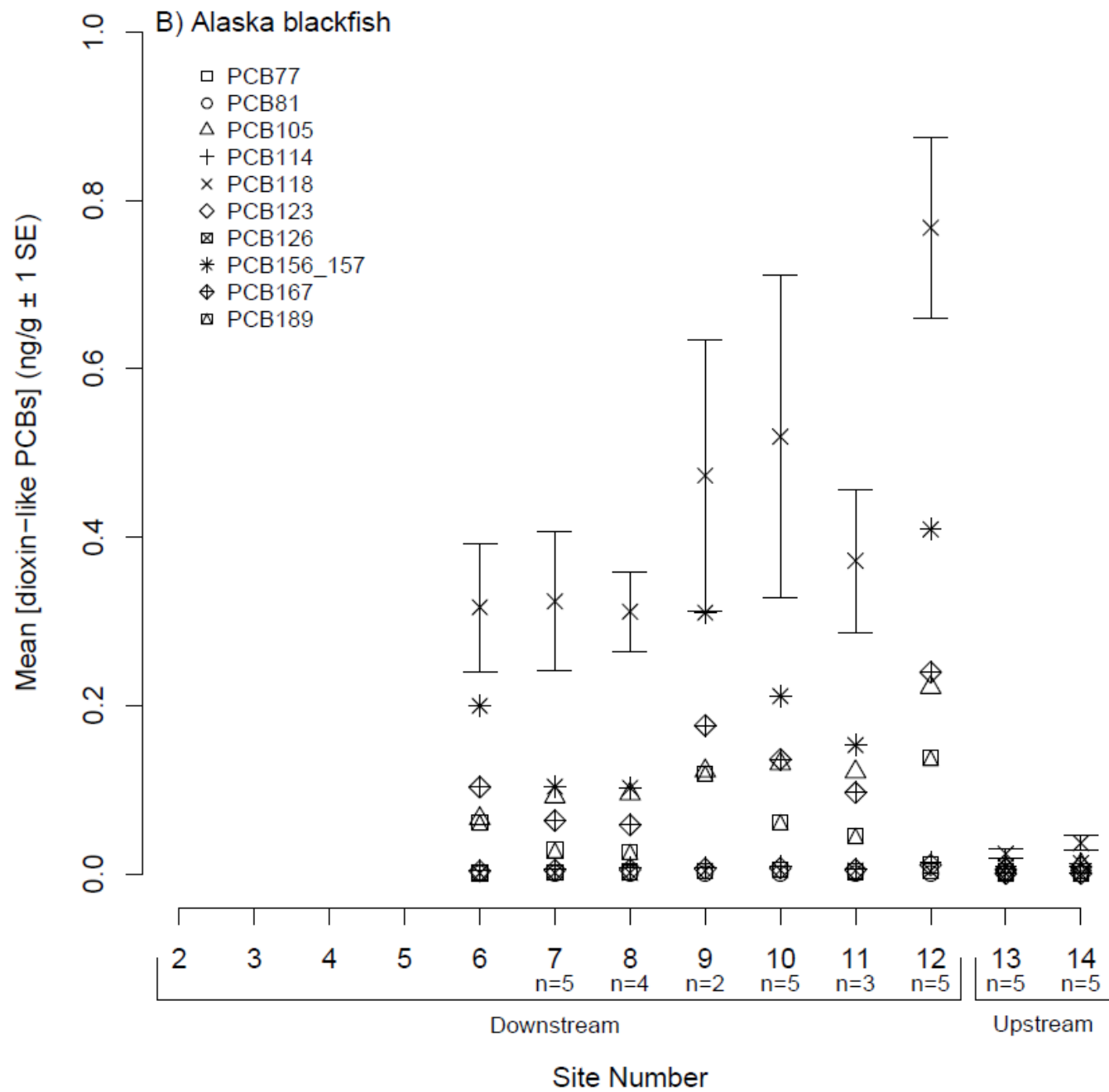


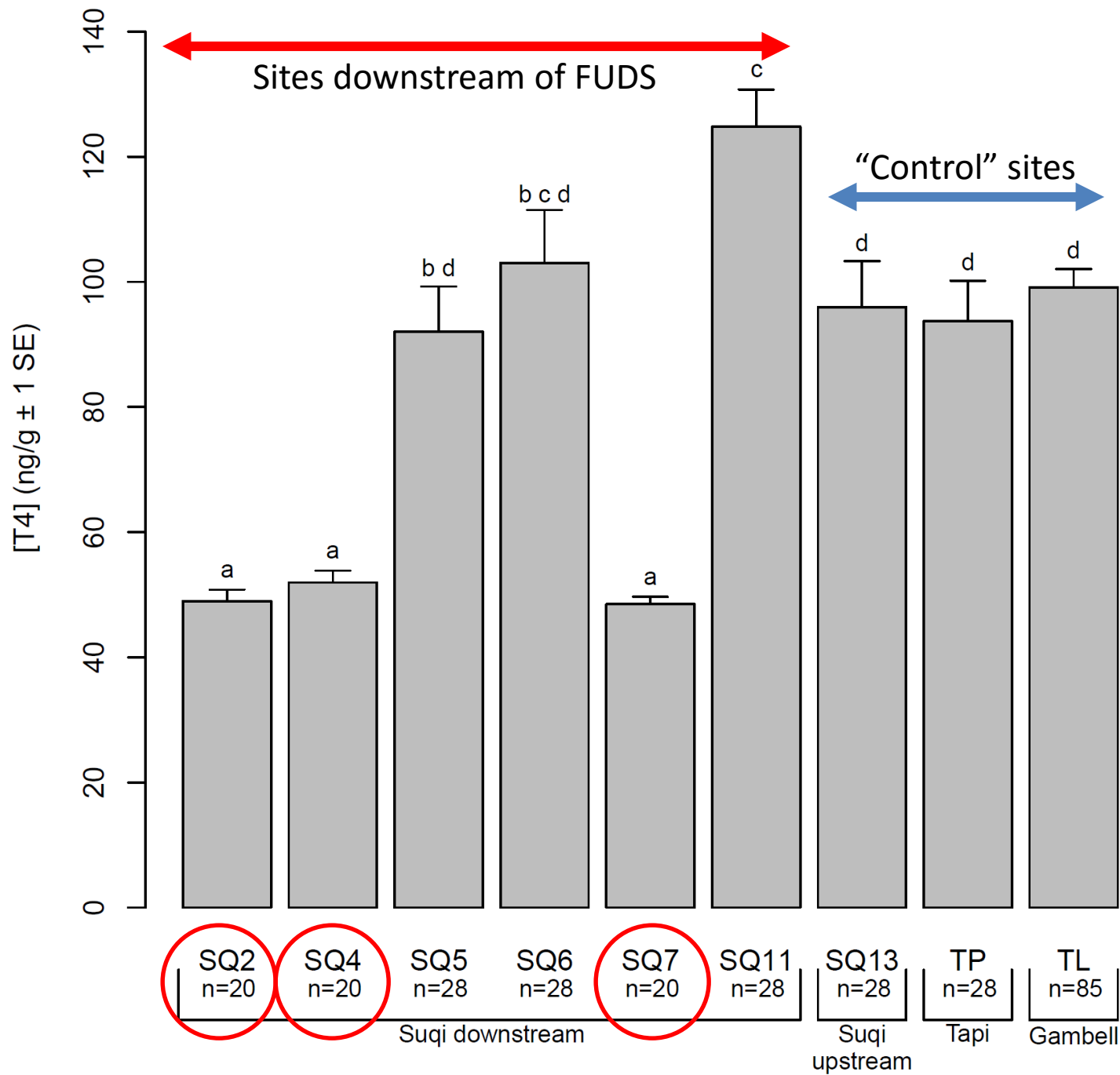
Is the endocrine system of the fish disrupted?





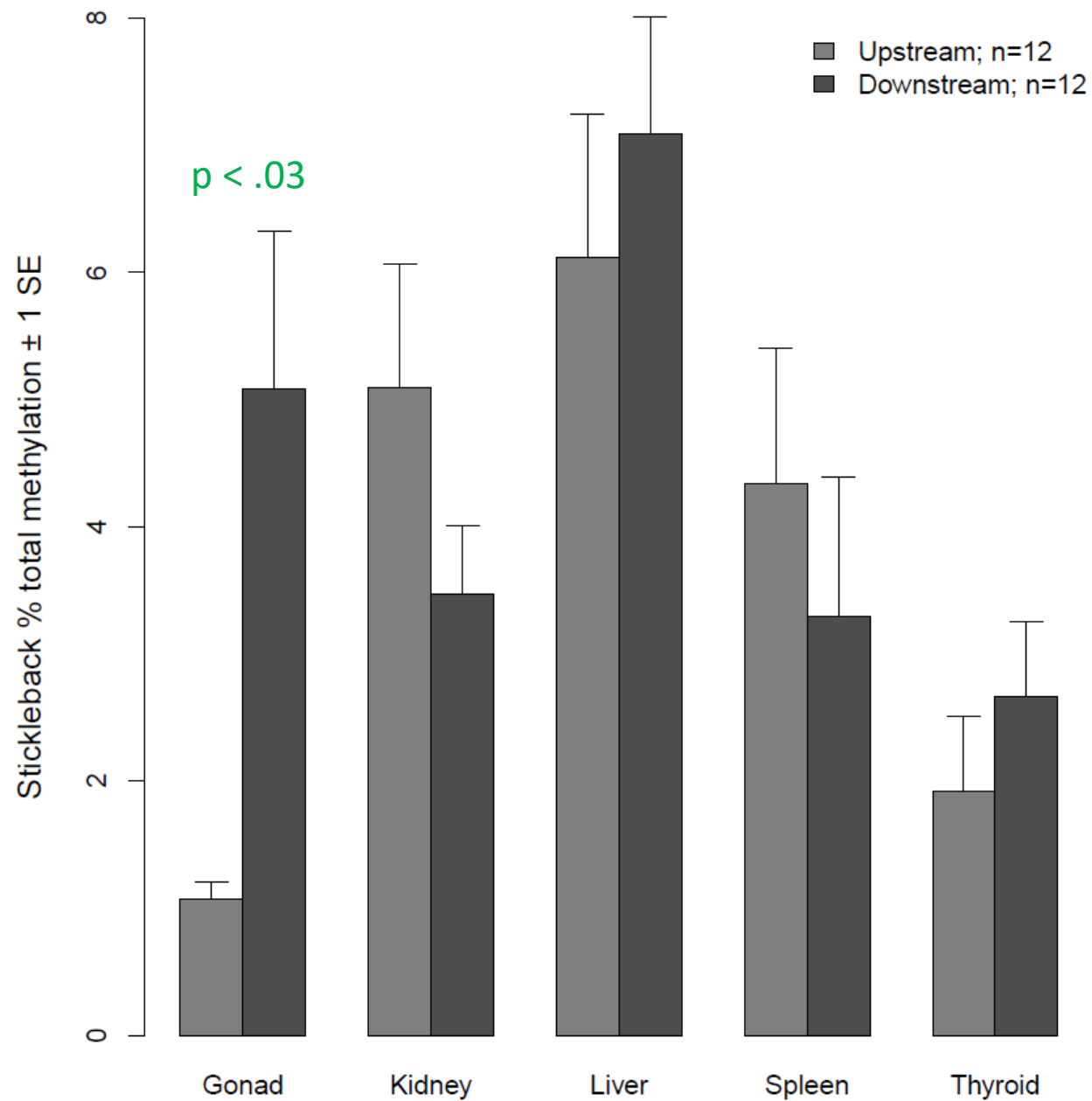






Is gene expression of the fish disrupted?





5-mC DNA ELISA Kit

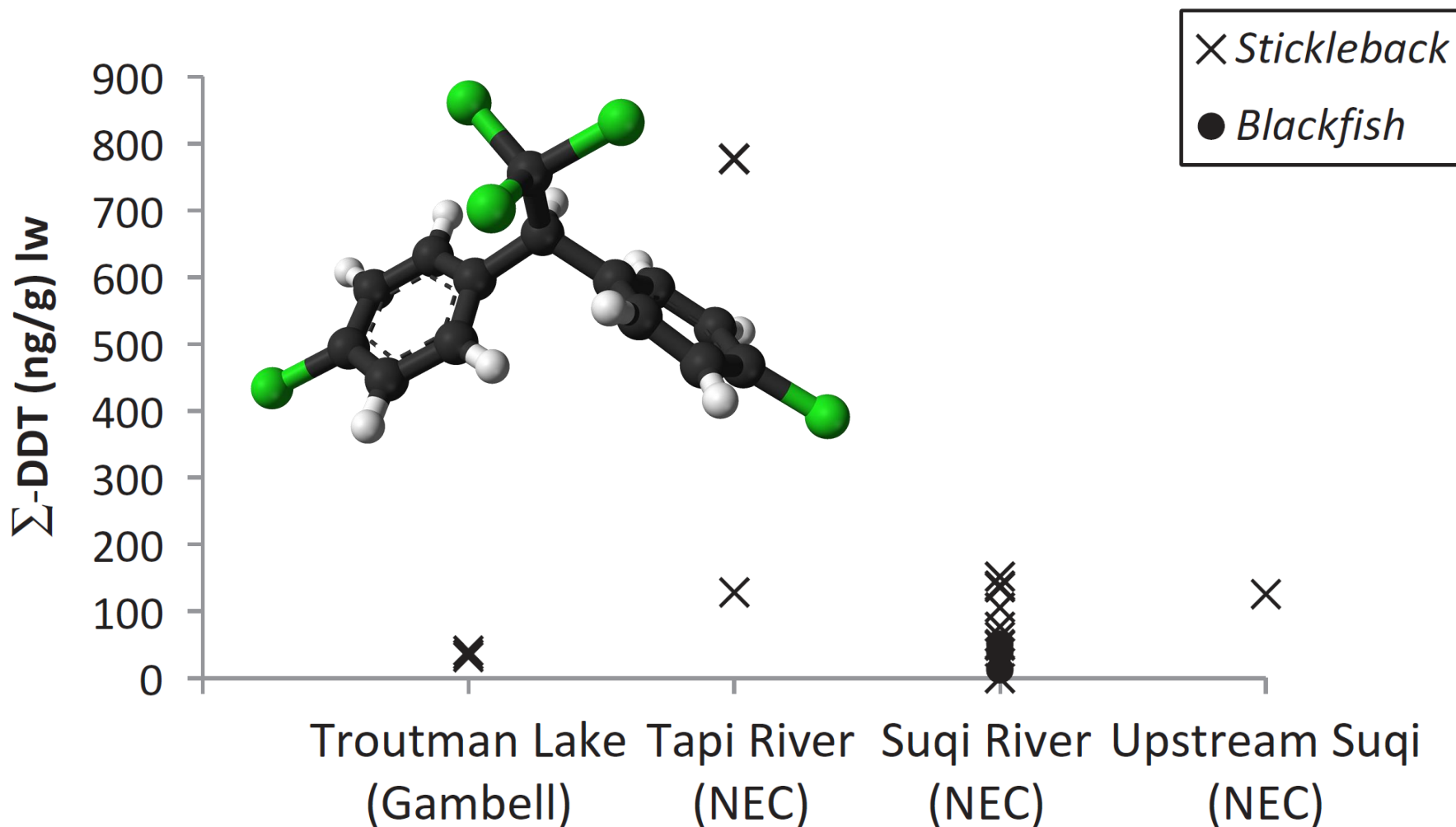
Gene expression results...

- Decreased expression of DNA repair genes could increase the accumulation of mutations and intensify the potential for carcinogenesis.
- Reduced cell signaling might exacerbate the risk of carcinogenesis by decreasing normal pathways of cell cycle arrest and apoptosis for genetically damaged cells.

Is Northeast Cape also associated with high pesticide levels?

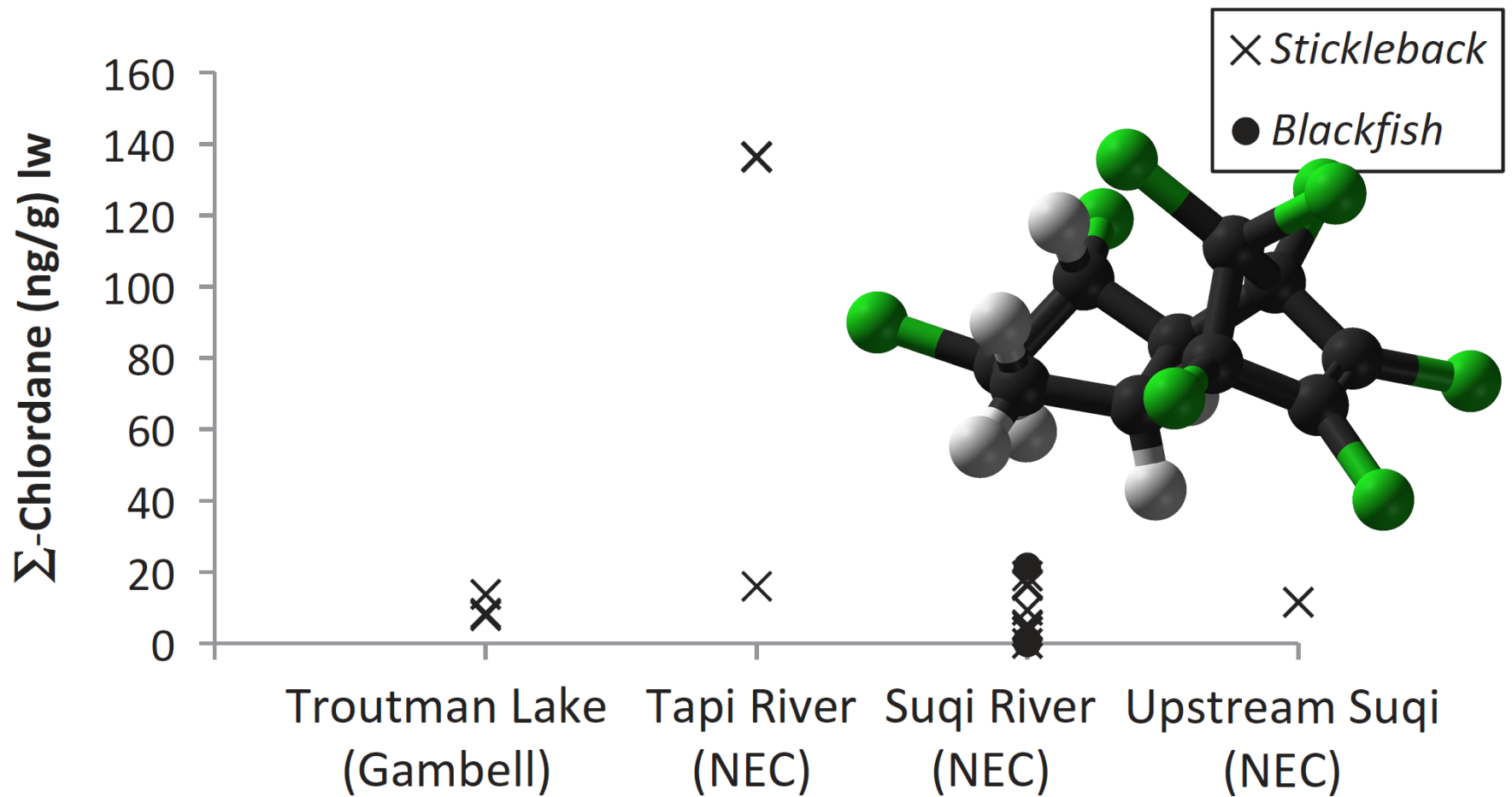


Insecticide, banned by the Stockholm Convention

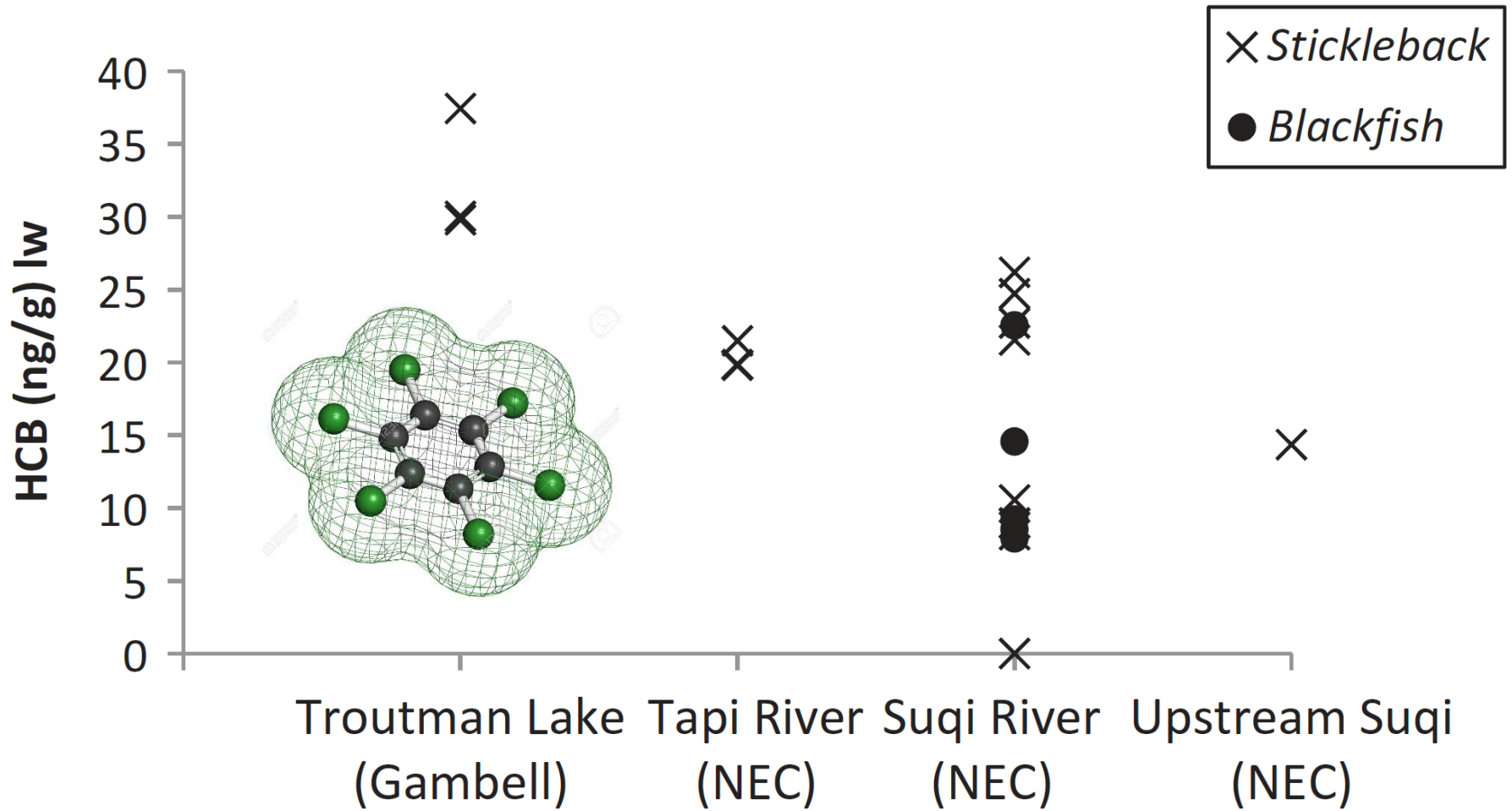


Byrne, S., Miller, P., Waghiyi, V., Buck, C.L., von Hippel, F.A. & Carpenter, D.O. (2015). Persistent organochlorine pesticide exposure related to a formerly used defense site on St. Lawrence Island, Alaska: data from sentinel fish and human sera. *Journal of Toxicology and Environmental Health, Part A* 78:1-16.

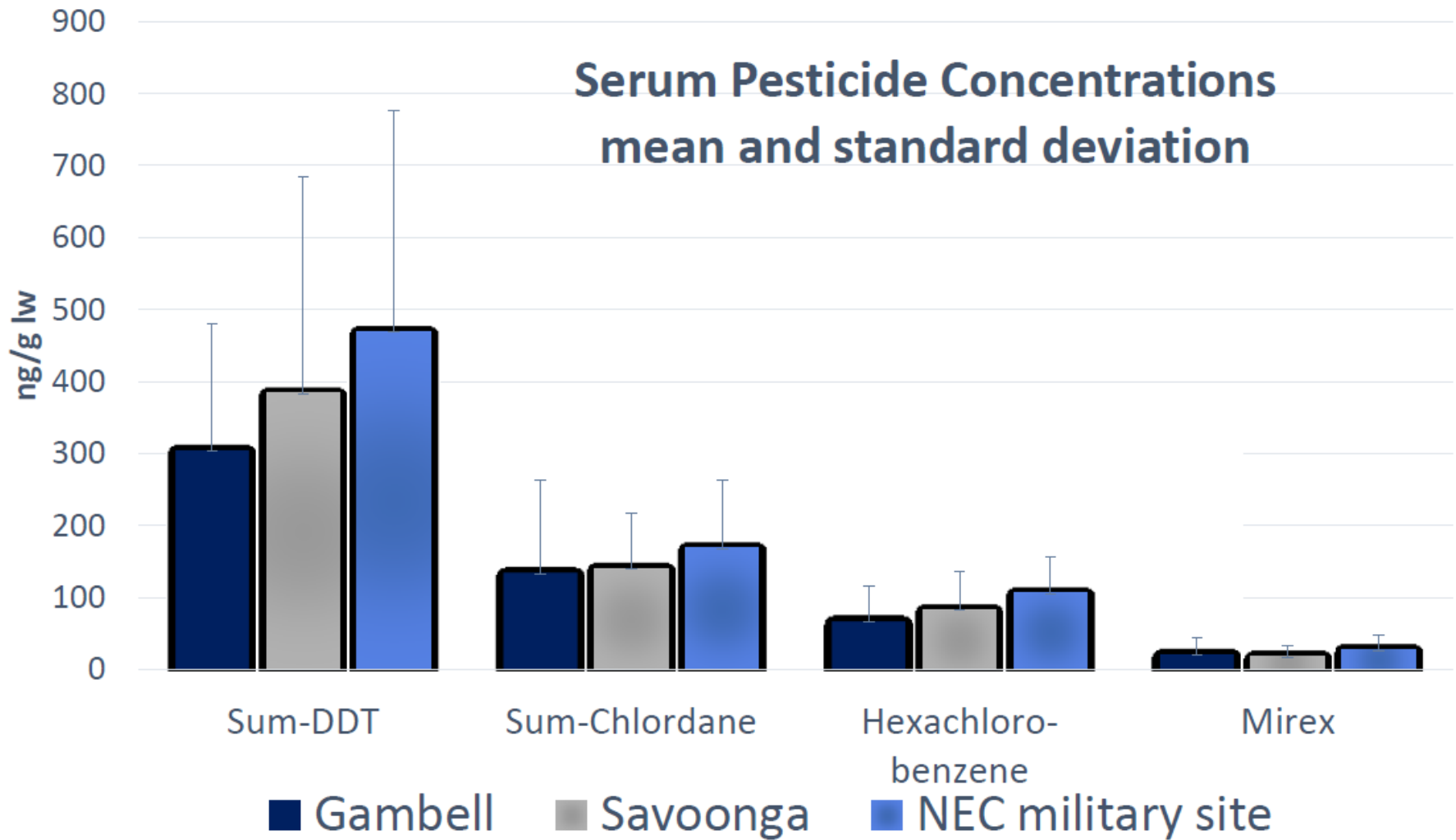
Insecticide, banned by the EPA



Fungicide, banned by the Stockholm Convention



Pesticides in blood serum of St. Lawrence Island residents

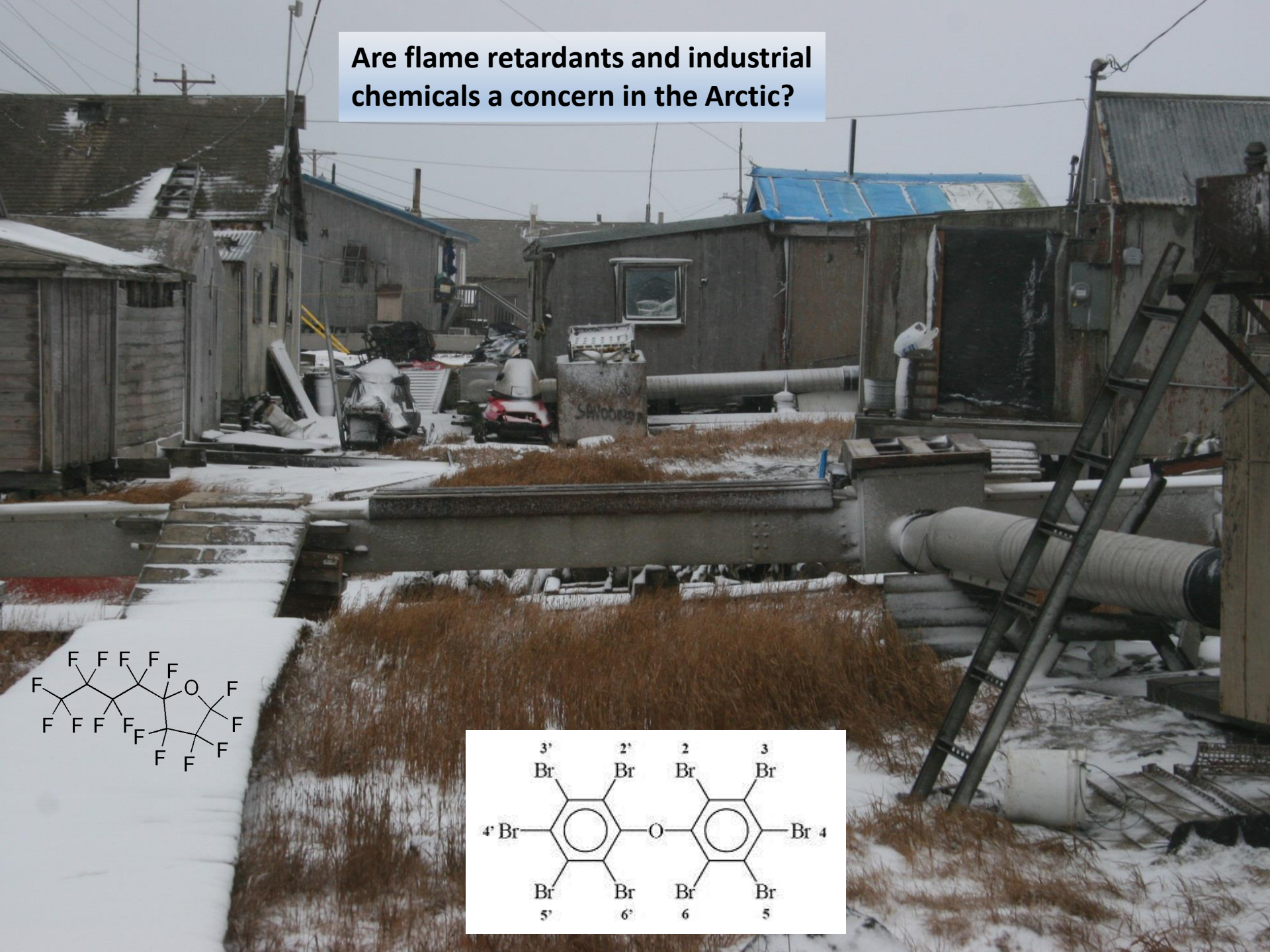
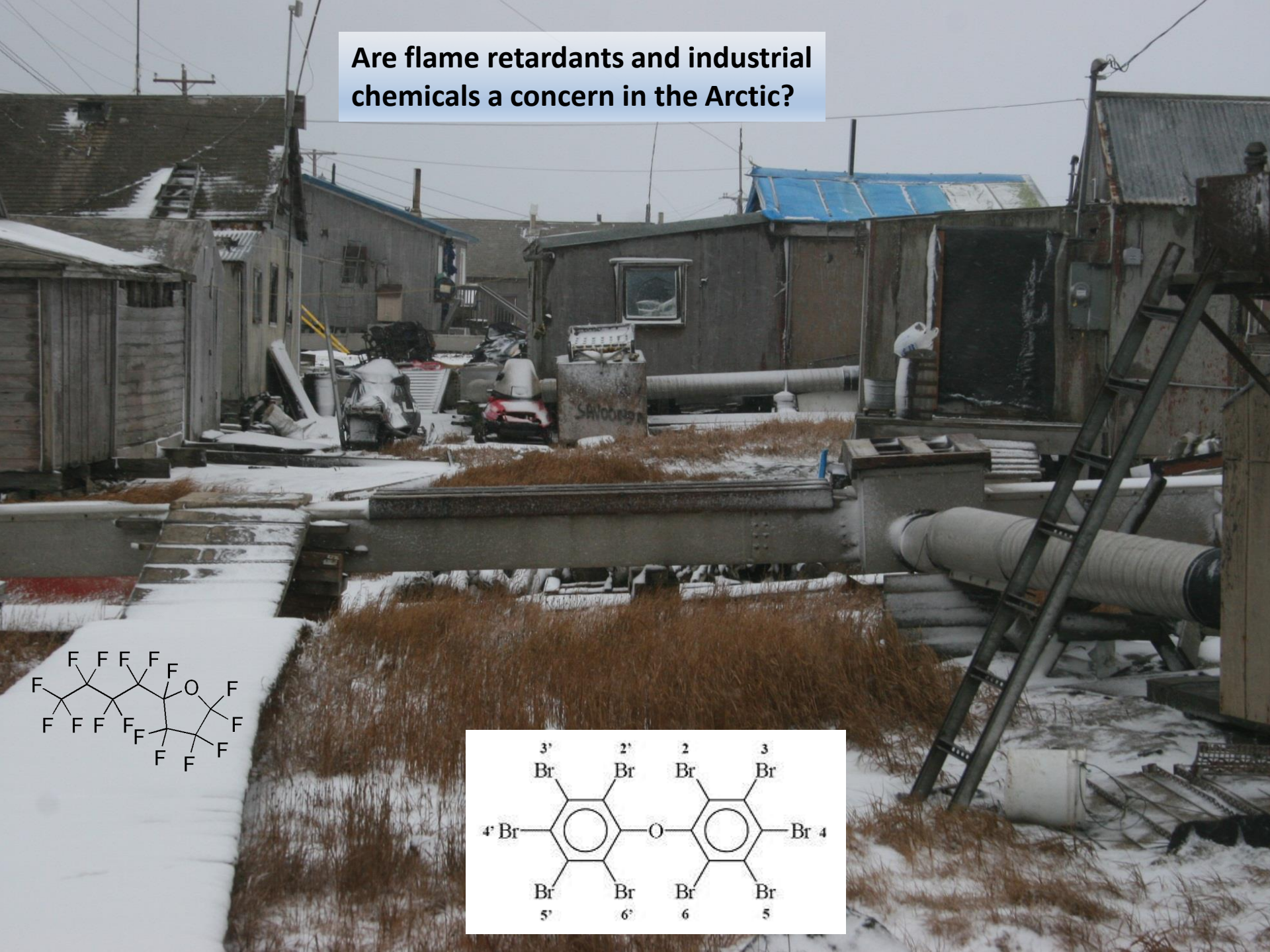


Are flame retardants and industrial chemicals a concern in the Arctic?

The image shows a snowy outdoor area with industrial or residential buildings. In the foreground, there is a snow-covered path and some dry grass. A large metal pipe runs horizontally across the middle ground. A ladder leans against a building on the right. The sky is overcast.

Chemical structures overlaid on the image:

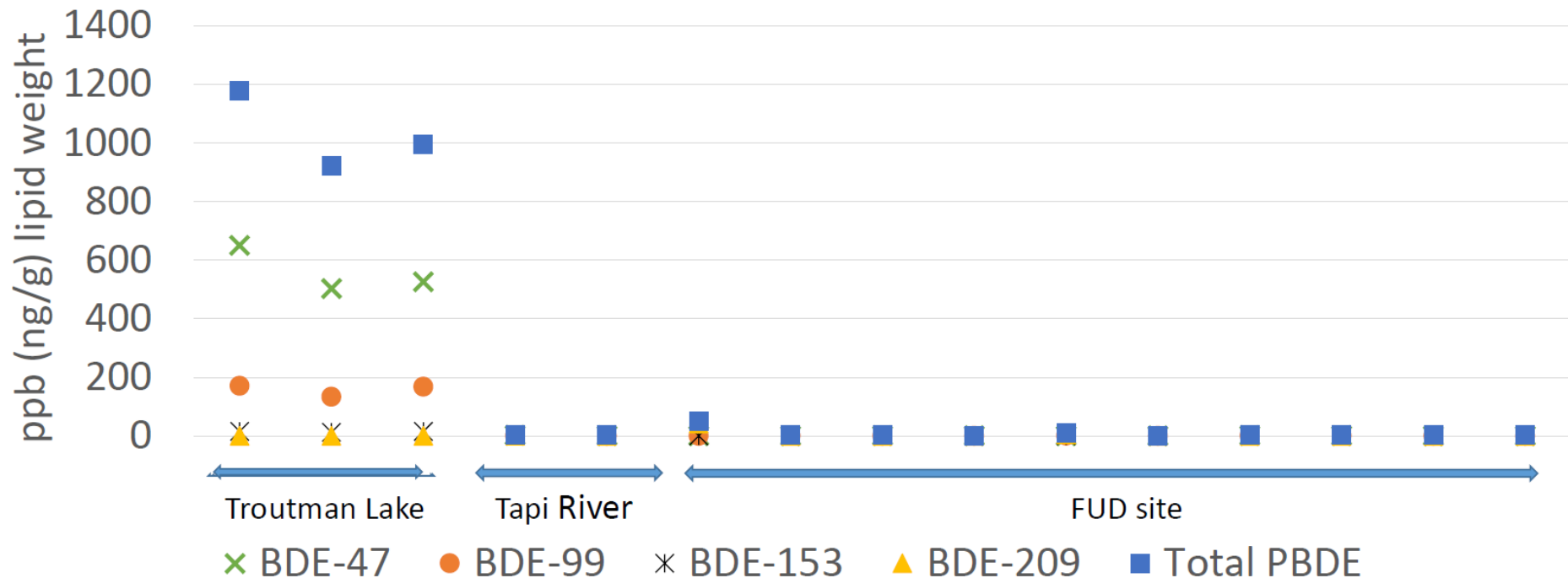
- Left structure:** A perfluorinated ether, specifically 1,1,1,2,2,2-hexafluoro-2-methoxyethane, with the chemical formula CF3CF2OCF3.
- Right structure:** A polybrominated diphenyl ether (PBDE), specifically 2,2',3,3',4,4',5,5'-octabromodiphenyl ether, with the chemical formula BrC1=CC(=C(C(=C1)Br)OC2=CC(=C(C(=C2)Br)Br)Br.





Byrne, S., Seguinot-Medina, S., Waghiyi, V., Miller, P.K., Buck, C., von Hippel, F.A. & Carpenter, D. (2017). Exposure to polybrominated diphenyl ethers and perfluoroalkyl substances in a remote population of Alaska Natives. *Environmental Pollution* 231:387-395.

PBDEs in stickleback



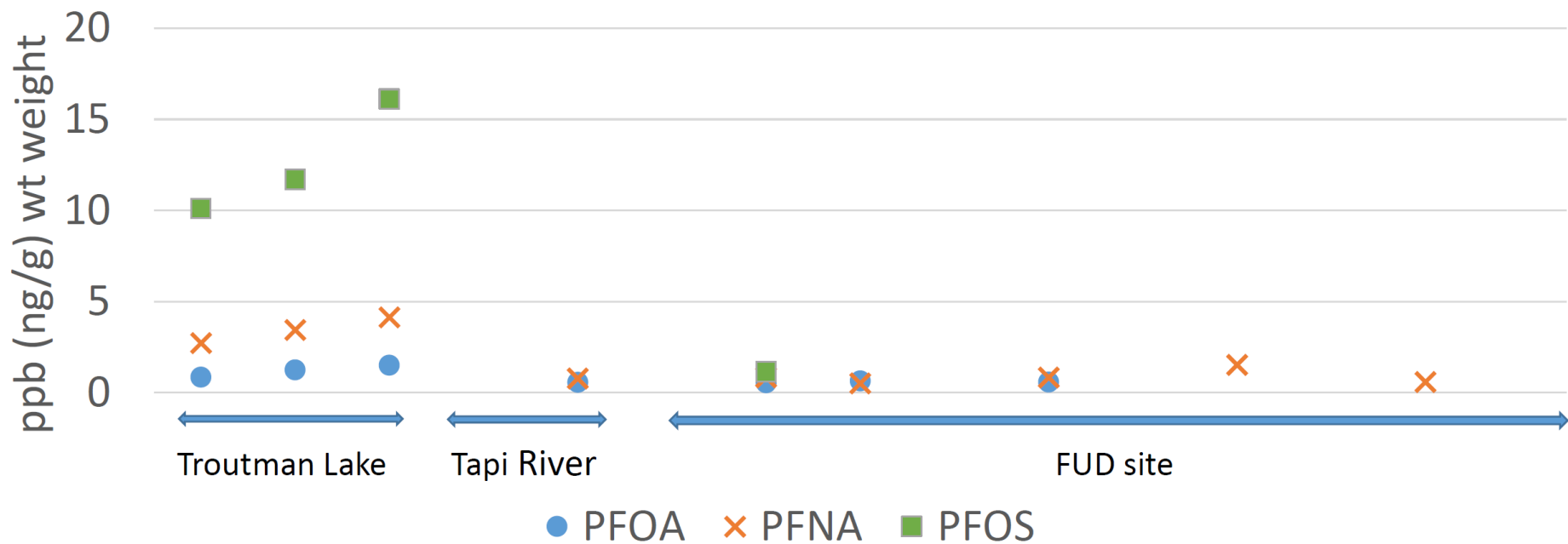


Troutman
Lake

Bering Sea

Gambell

PFASs in stickleback



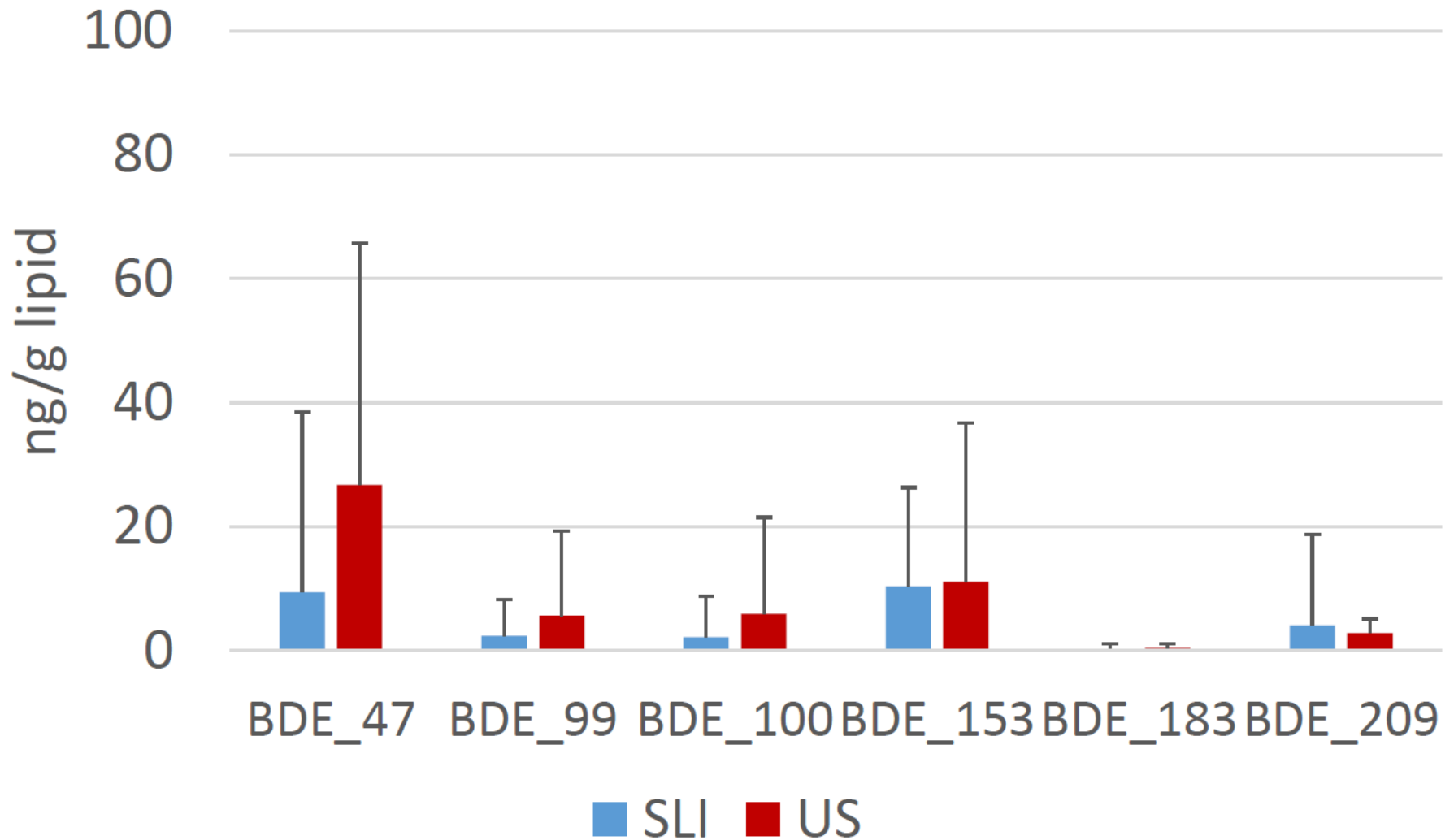
We find high levels of PBDEs & PFASs in stickleback from Gambell; is this reflected in household dust, subsistence foods & human blood serum?



Gambell: Women – 23; Men - 15
Savoonga: Women - 25; Men – 22
85 Individuals in 50 households.

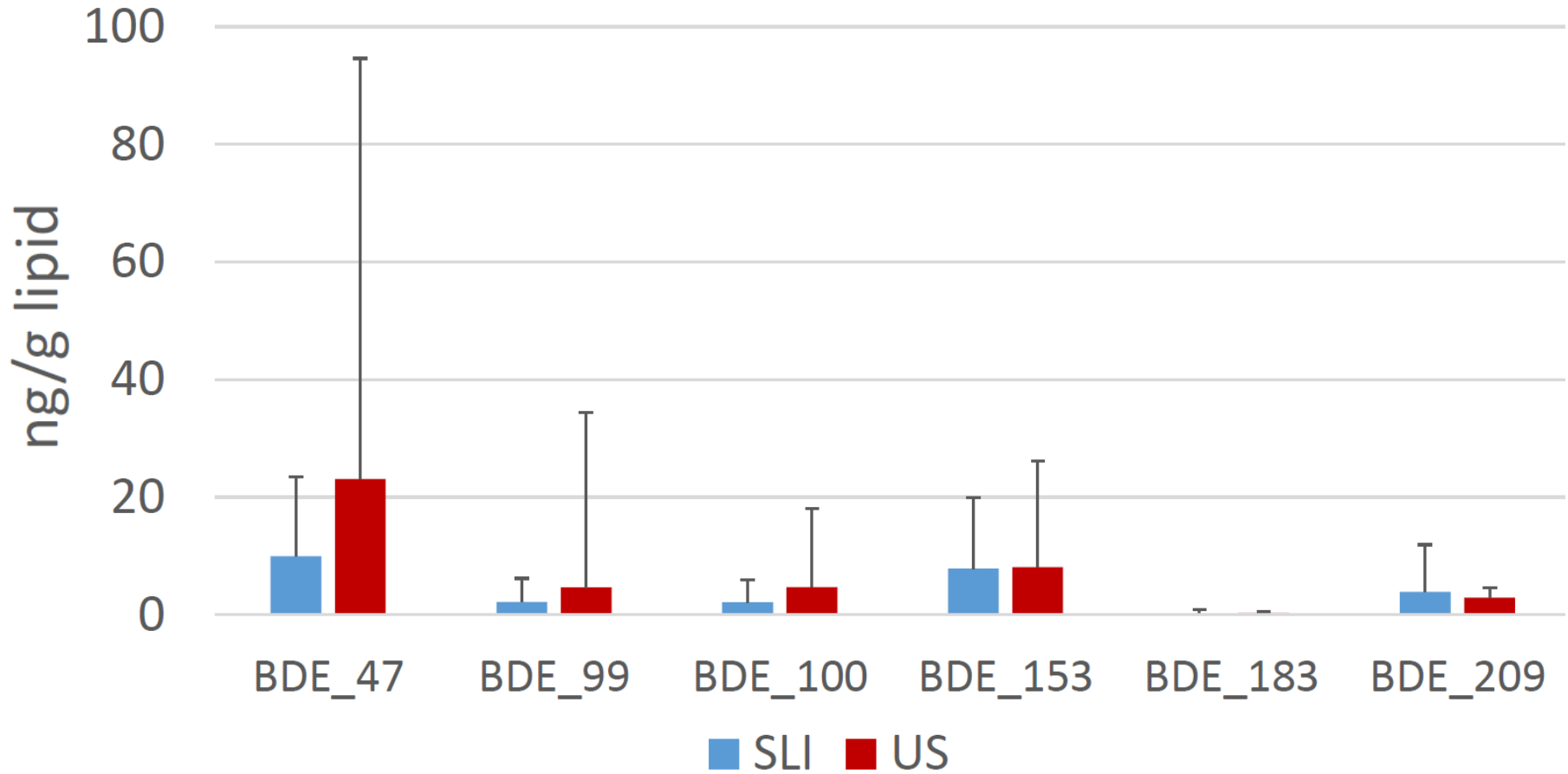
PBDEs in blood serum of St. Lawrence Island men

median & 95th percentiles

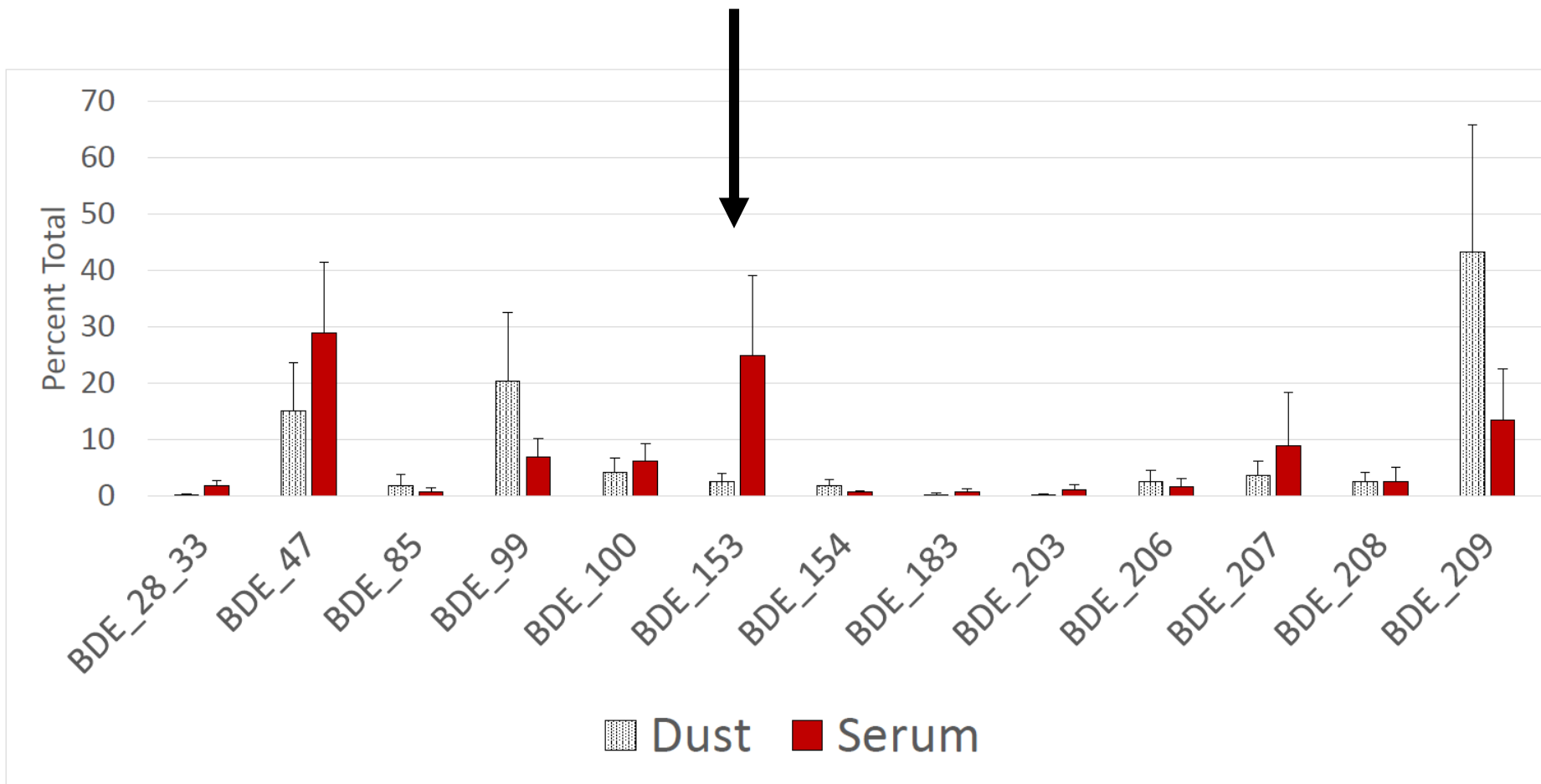


PBDEs in blood serum of St. Lawrence Island women

median & 95th percentiles

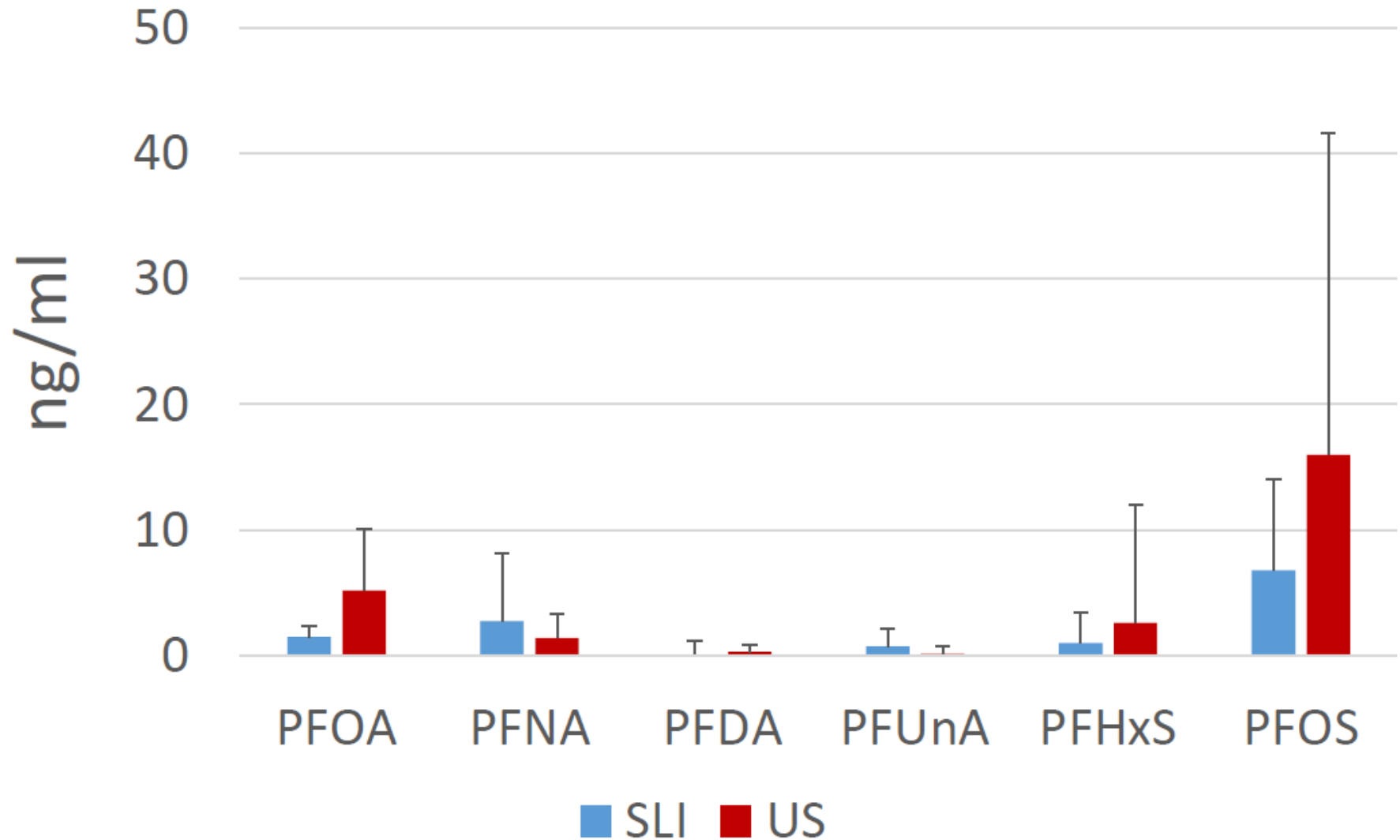


Relative concentrations in dust & serum



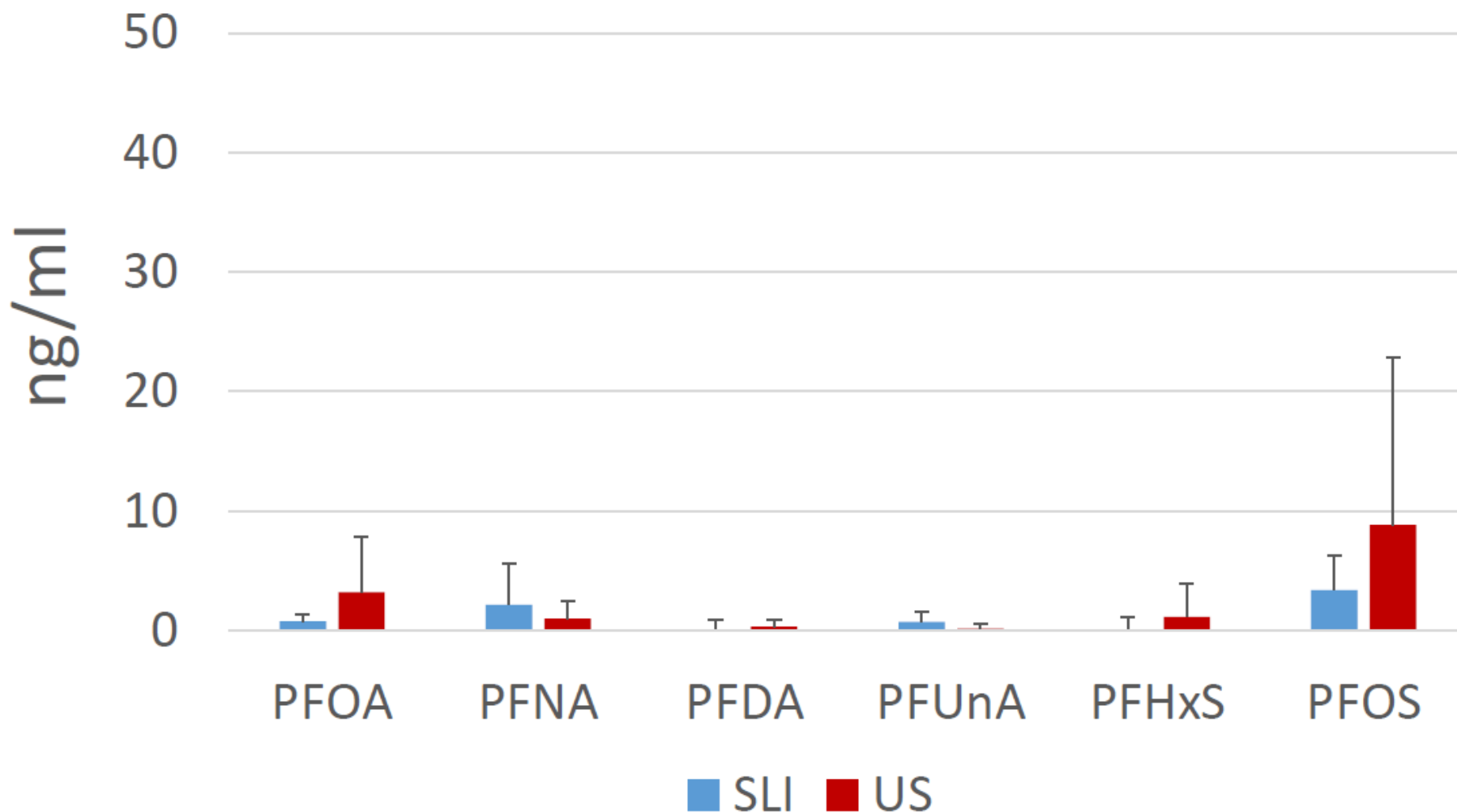
PFASs in blood serum of St. Lawrence Island men

median & 95th percentiles

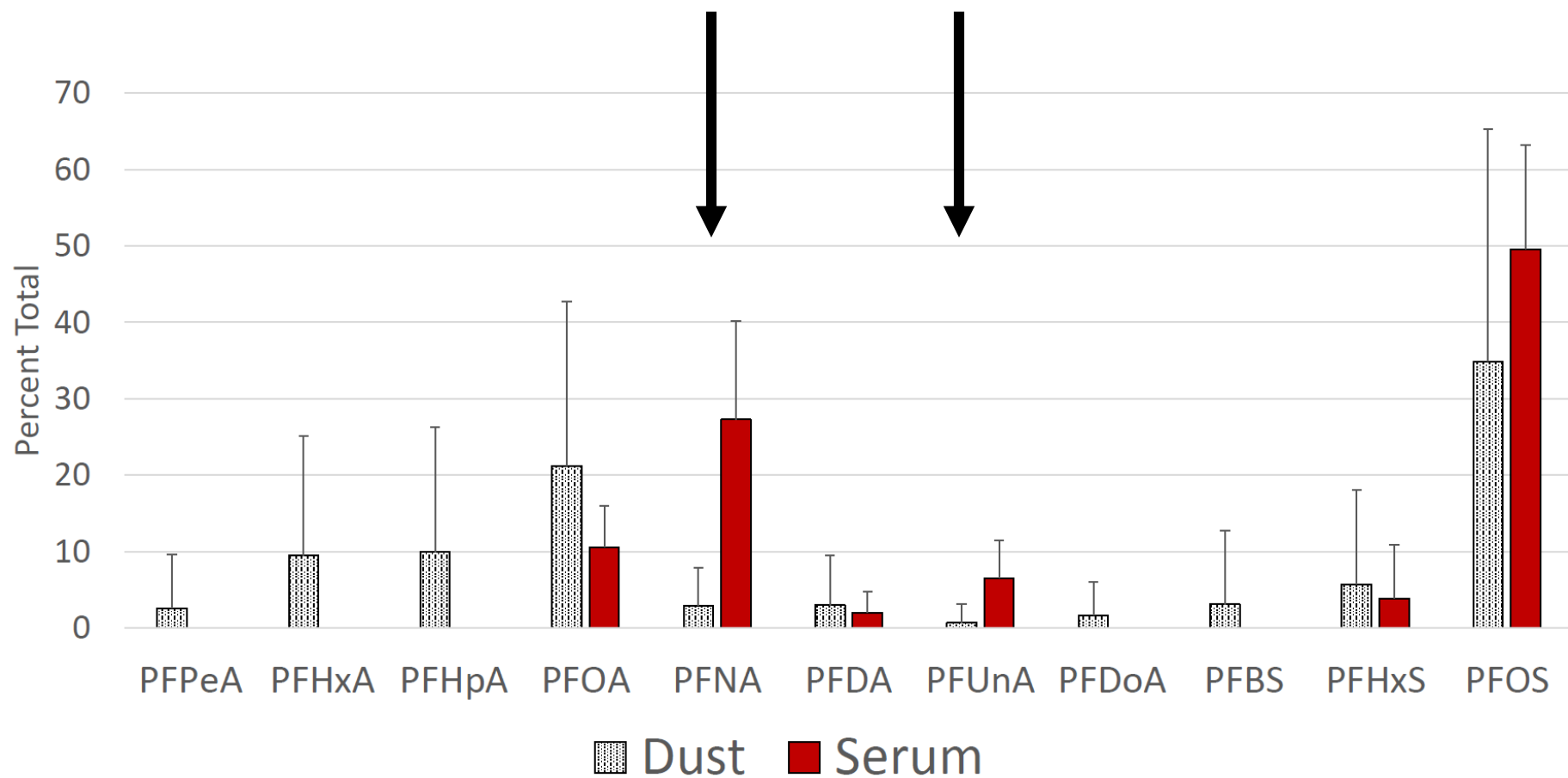


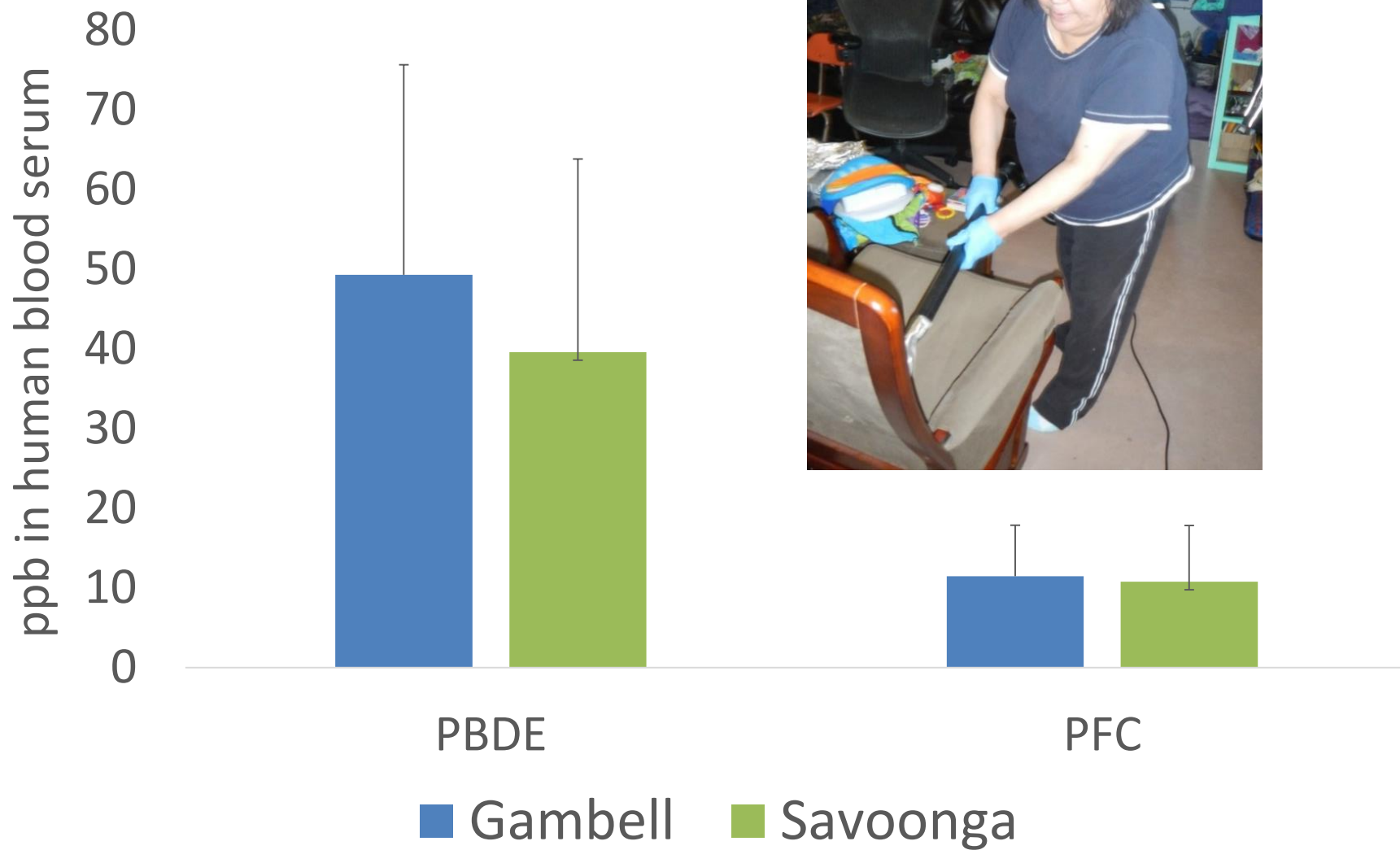
PFASs in blood serum of St. Lawrence Island women

median & 95th percentiles



Relative concentrations in dust & serum





Serum [BDE-28/33, 47, and 100] positively associated with [TSH] and [free T3], while serum [BDE-153] negatively associated with [total T3]



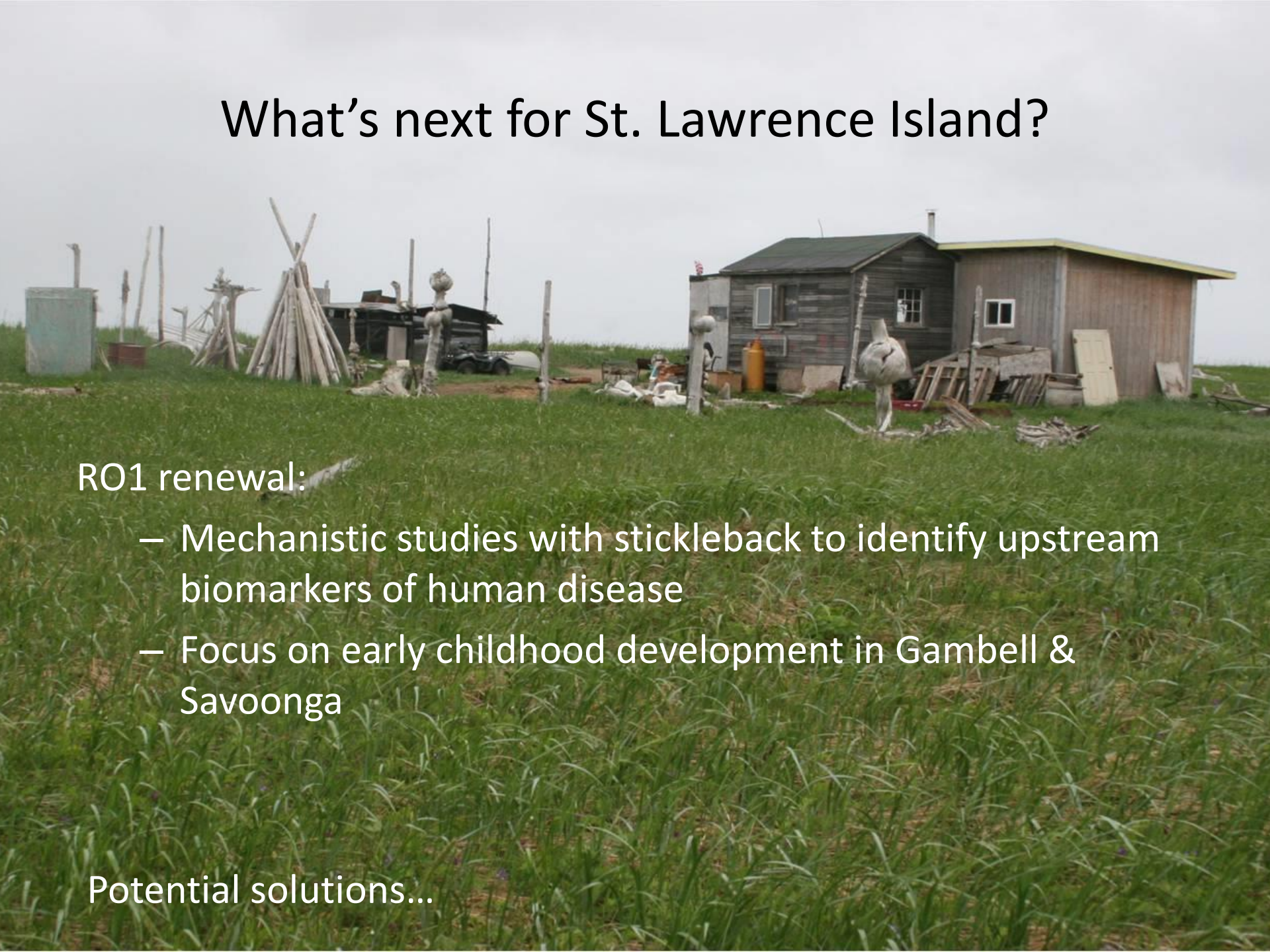
Byrne, S.C., Miller, P., Seguinot-Medina, S., Waghiyi, V., Buck, C.L., von Hippel, F.A. & Carpenter, D.O. (2018). Associations between serum polybrominated diphenyl ethers and thyroid hormones in a cross sectional study of a remote Alaska Native population. *Scientific Reports* 8:2198.

What's next for St. Lawrence Island?

RO1 renewal:

- Mechanistic studies with stickleback to identify upstream biomarkers of human disease
- Focus on early childhood development in Gambell & Savoonga

Potential solutions...

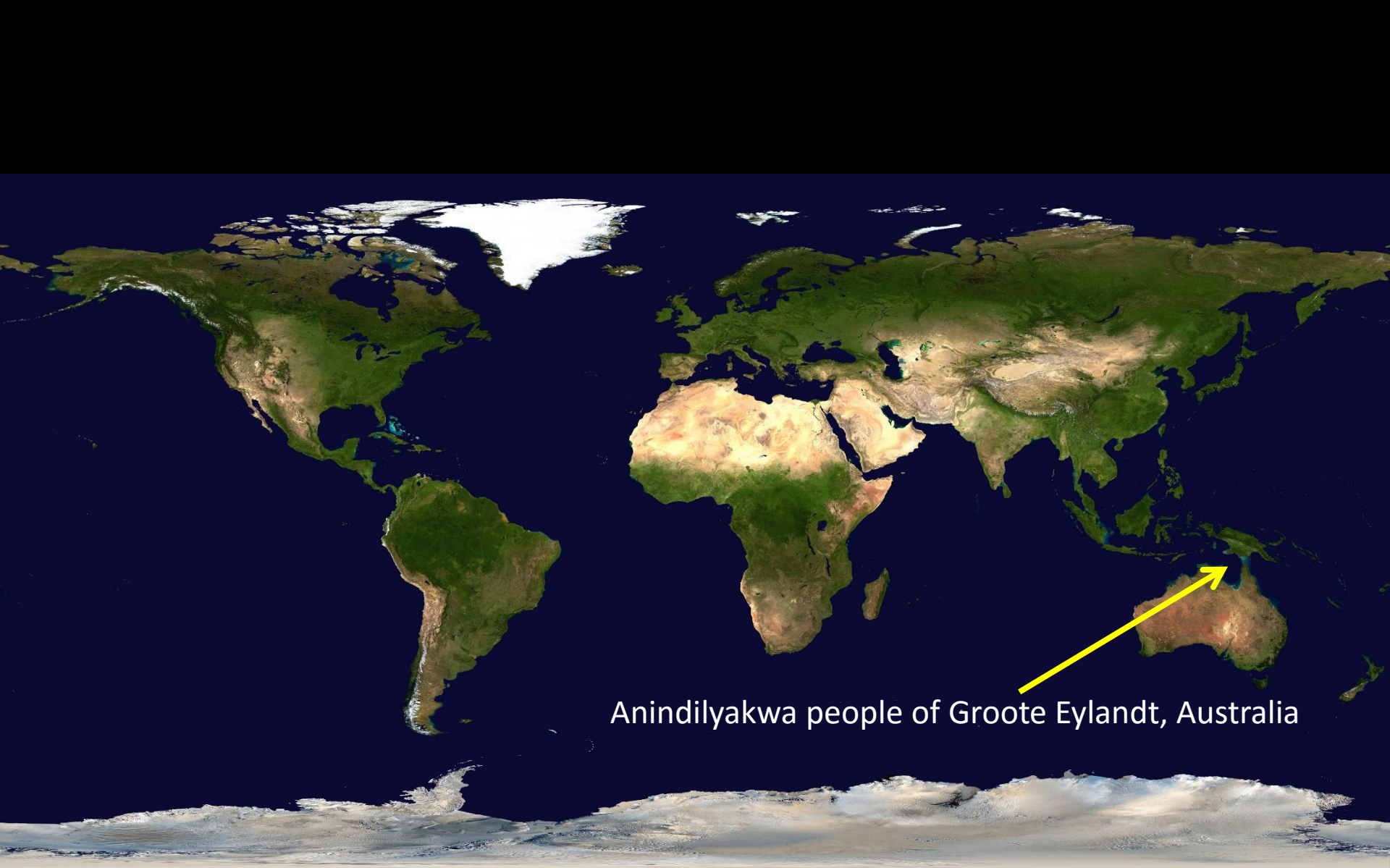


Practical implications for arctic communities



Environmental remediation standards

Prevalence of contaminated sites throughout the Arctic
CBPR is informing policy at the local, state, national, and
international levels



Anindilyakwa people of Groote Eylandt, Australia



What is the problem?



Angurugu



performance biology: Robbie Wilson & Ph.D. student Ami Fadhilah Amir Abdul Nasir
ecotoxicology: Frank von Hippel
gene expression: John Postlethwait
endocrinology: Loren Buck

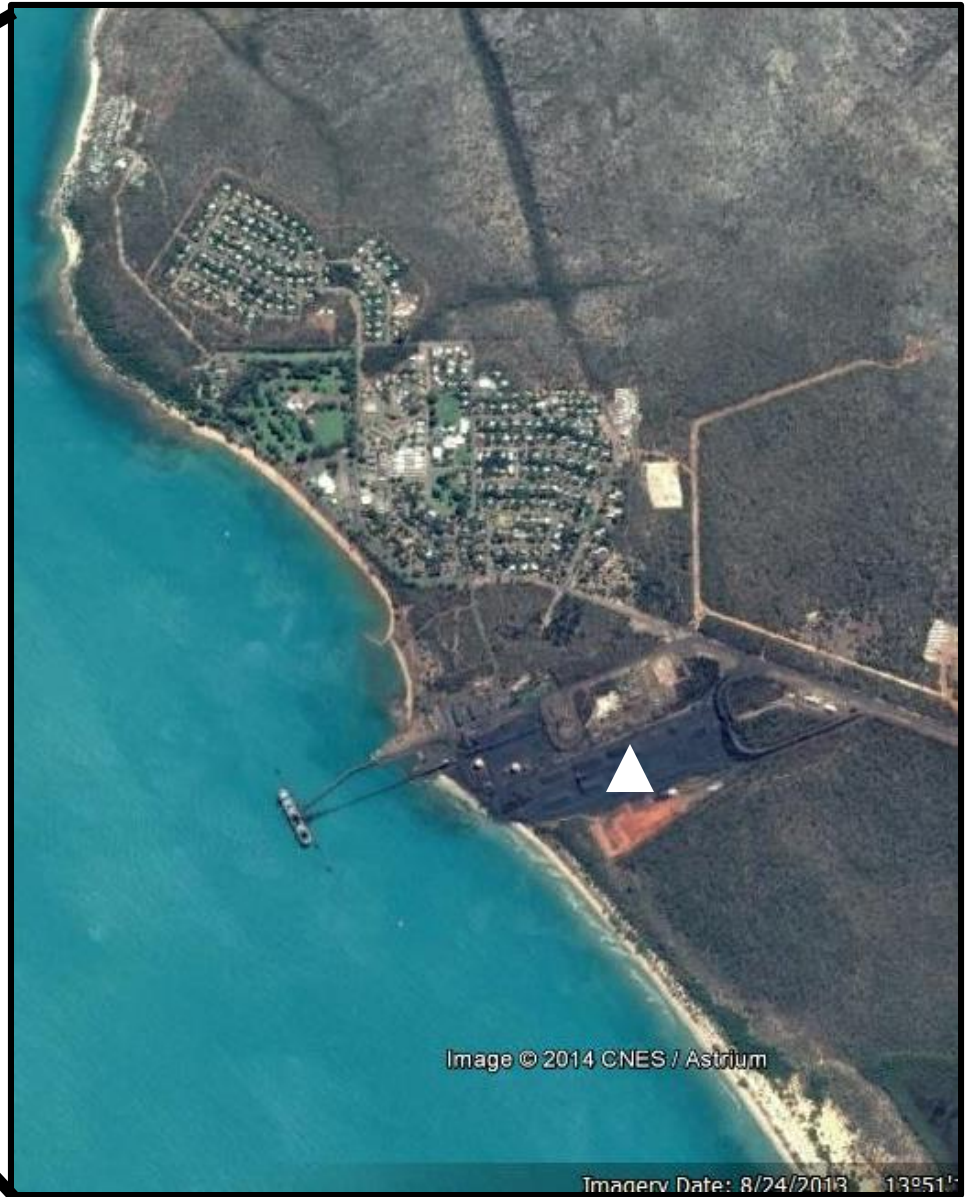
CAUTION

**LONG WIDE HAULAGE TRUCKS
USING ROAD 24 HRS A DAY**

49 METRES LONG



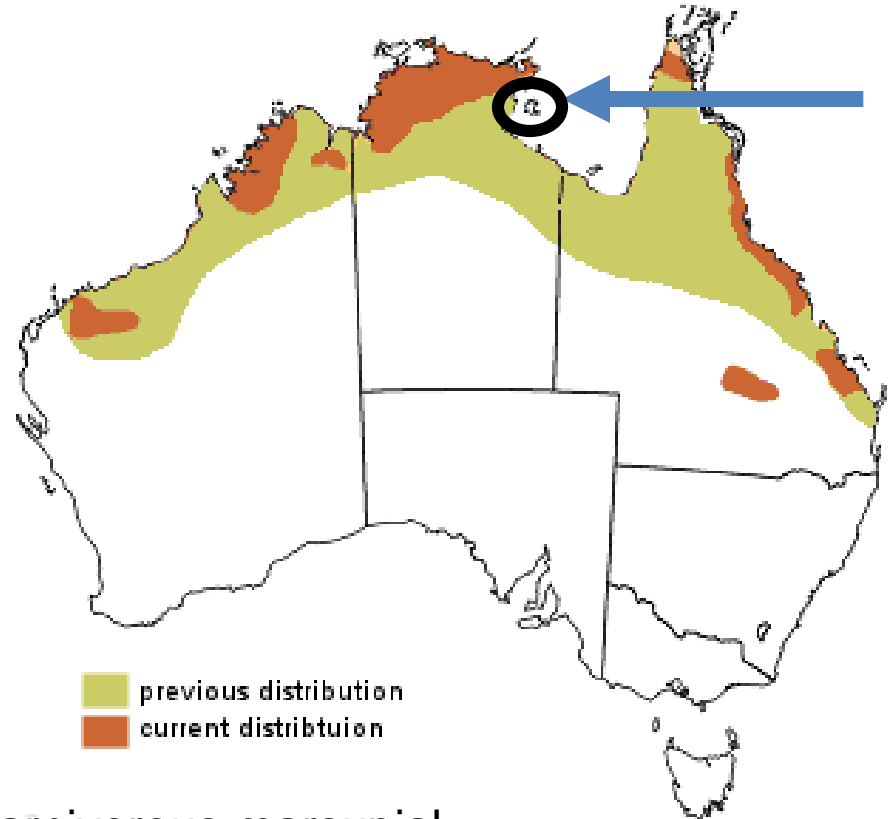




Alyangula



northern quoll (*Dasyurus hallucatus*)



carnivorous marsupial
diverse habitats, partially arboreal
0.3 – 1.2 kg
endangered

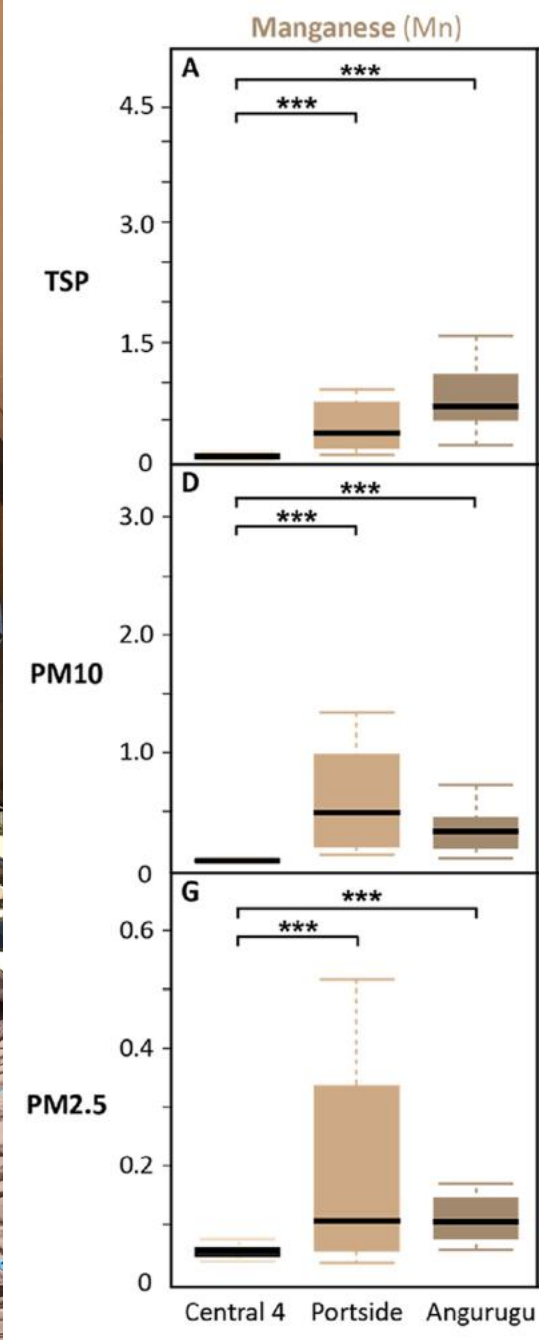
Funding from the Anindilyakwa Land Council
& the Australian Research Council



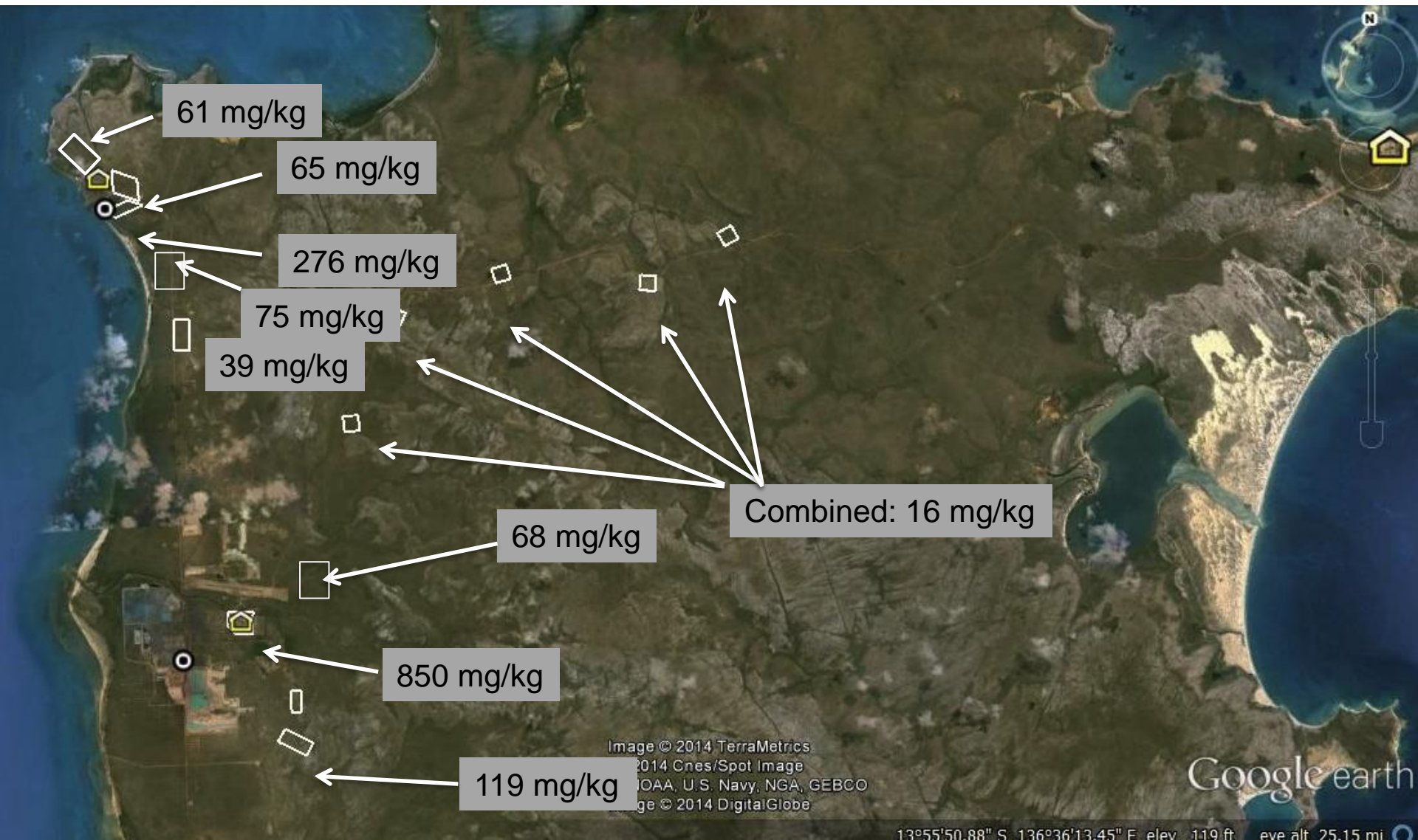
Is the level of Mn in the air near the mine (Angurugu) and at the port higher than elsewhere on the island?

Amir Abdul Nasir, A.F., Cameron, S.F., von Hippel, F.A., Postlethwait, J.H., Niehaus, A.C., Blomberg, S. & Wilson, R.S. (2018). Manganese accumulates in the brain of northern quolls (*Dasyurus hallucatus*) living near an active mine. *Environmental Pollution* 233:377-386.

Amir Abdul Nasir, A.F., Cameron, S.F., von Hippel, F.A., Postlethwait, J.H., Niehaus, A.C., Blomberg, S. & Wilson, R.S. (2018). Manganese accumulates in the brain of northern quolls (*Dasyurus hallucatus*) living near an active mine. *Environmental Pollution* 233:377-386.



Do quolls bioaccumulate Mn based on location relative to the mine?

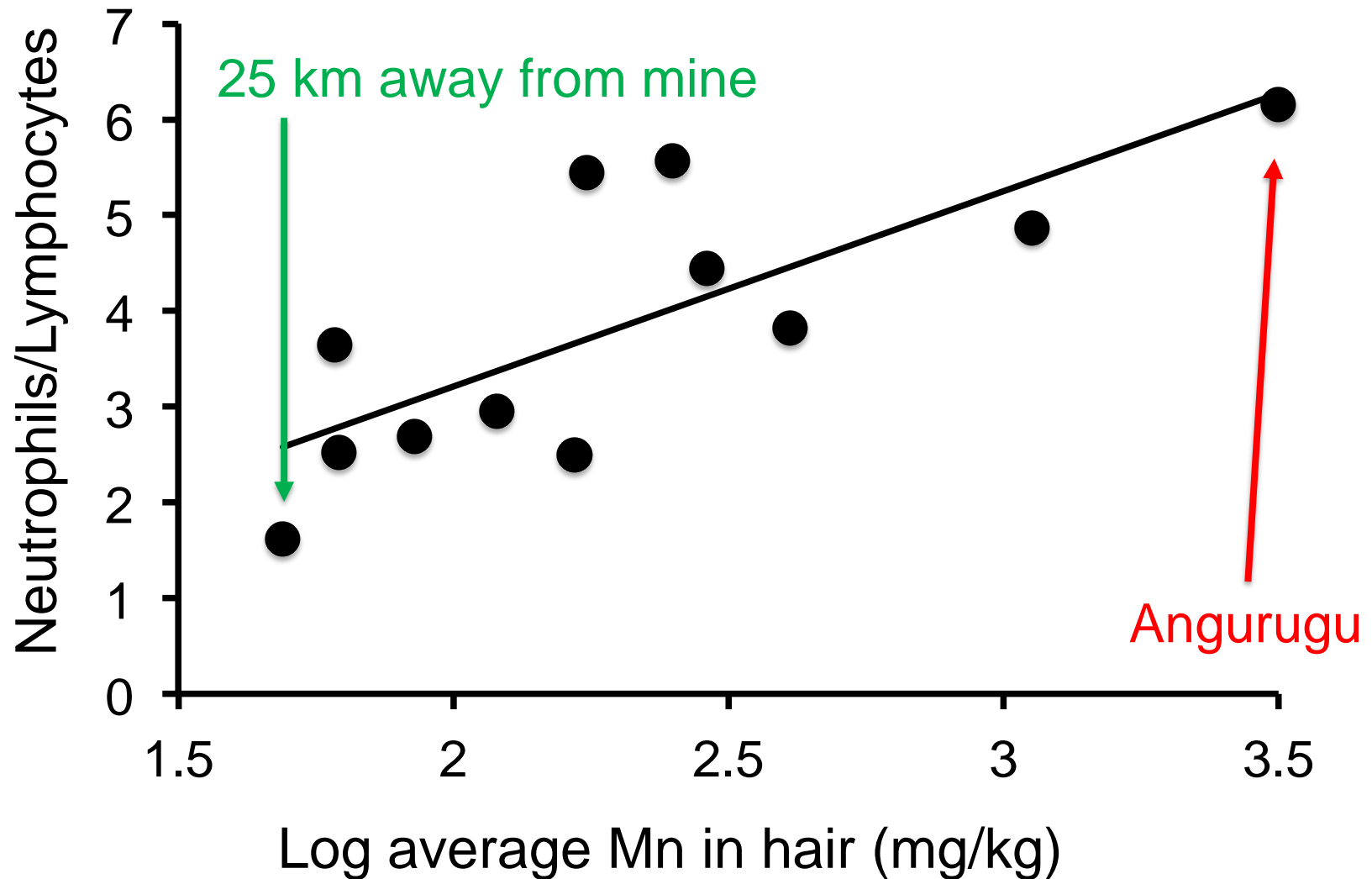


Manganese concentration in hair of 142 quolls – 2014



What is the relationship between [Mn]
and the health of the quolls?

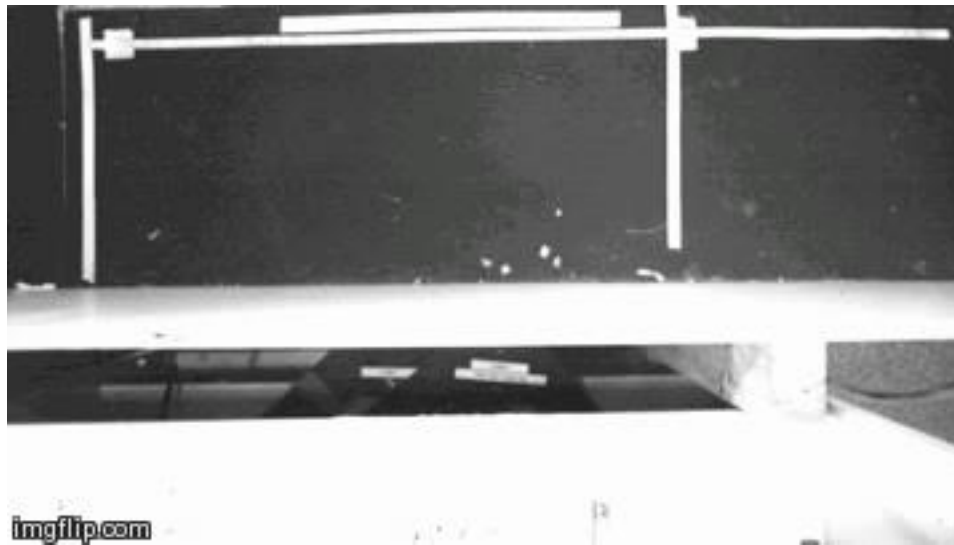
Quolls near the mine are in poorer health (n=115 quolls)



Mn accumulation was associated with reduced immune function (based on bacterial killing capacity by plasma)

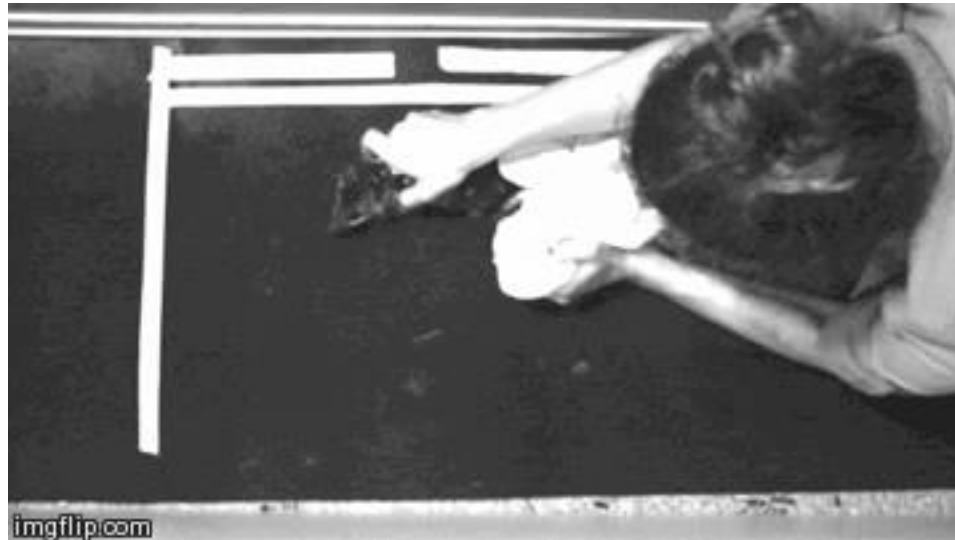
Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 1. Sprint Speed



Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 1. Acceleration



Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:

3. Bite Force



Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 1. Growth
 2. Feed Efficiency
 3. Feed Conversion Ratio
 4. Grasp Strength



Mn appears to affect immune function, but is it related to critical performance traits?

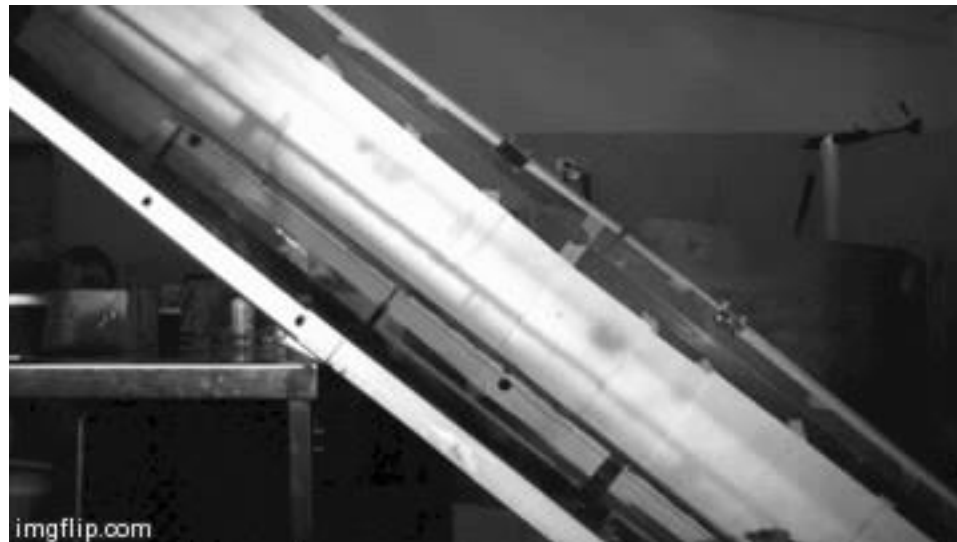
- 8 performance traits:

5. Jump Power



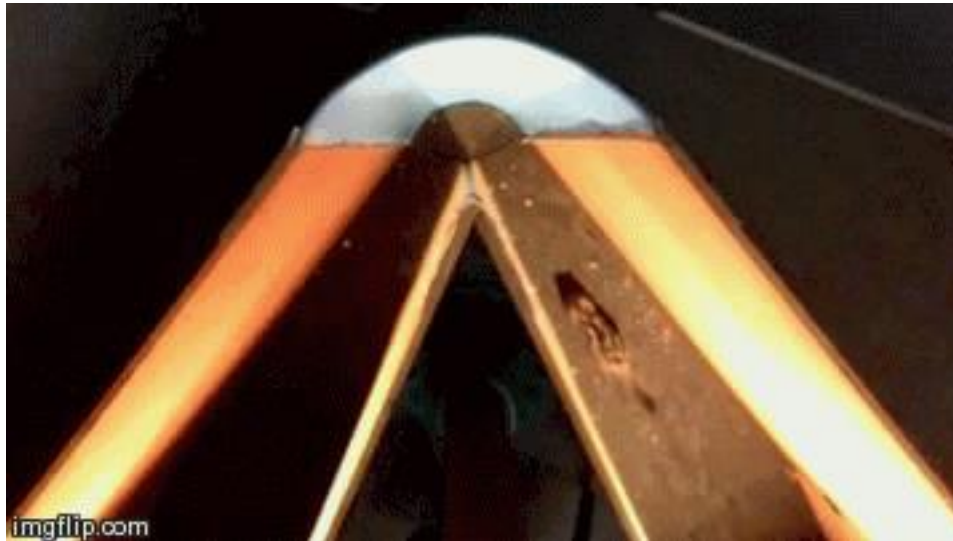
Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 - 6. Beam Running Speed



Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 - 7. Average Corner Speed



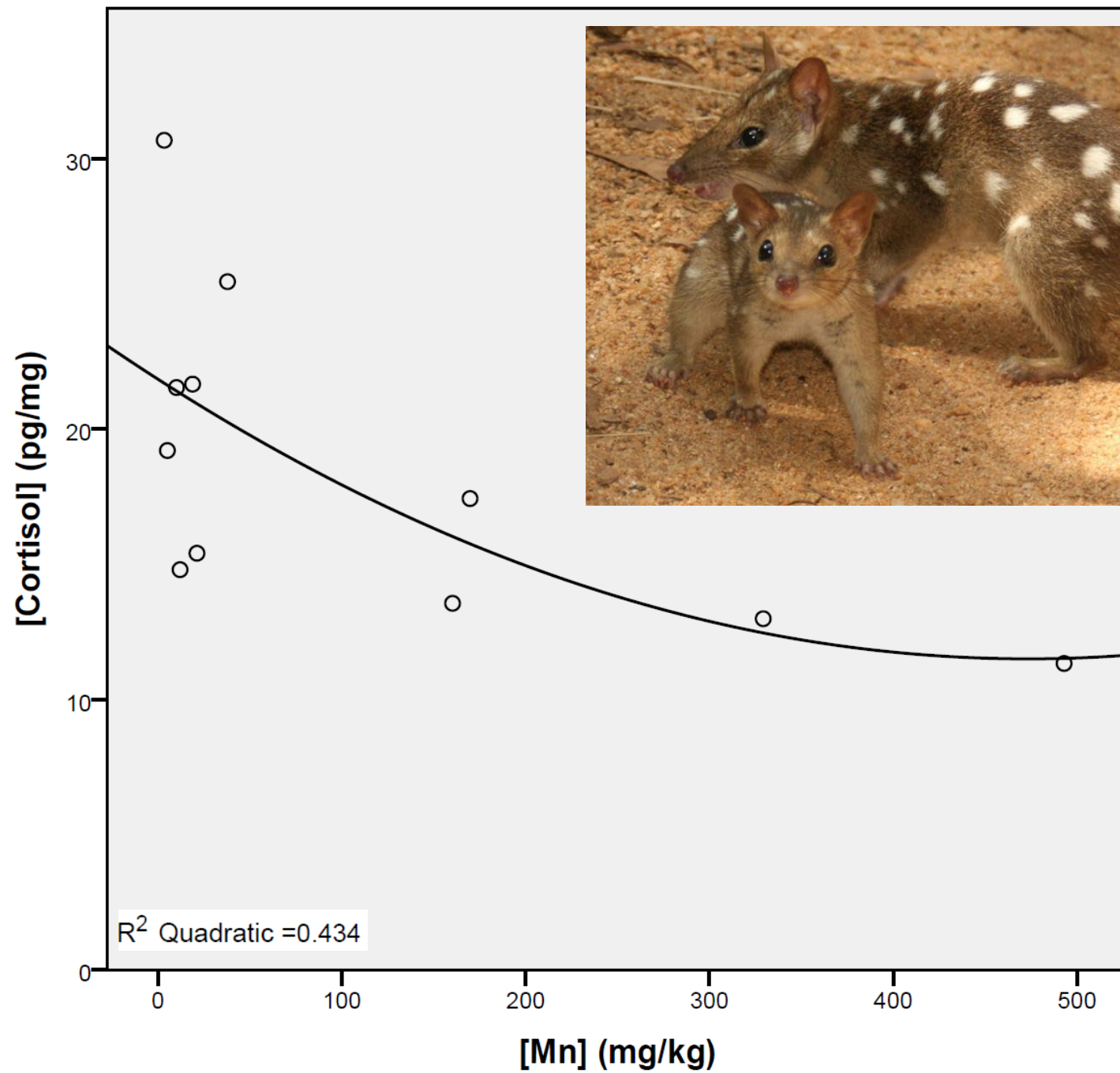
Mn appears to affect immune function, but is it related to critical performance traits?

- 8 performance traits:
 1. Maximum Oxygen Consumption





Does Mn disrupt endocrine function in quolls?




How does Mn affect the expression of genes involved in locomotion, cognition, immune function, etc.?



tissue tropism, gene expression, histology:

n = 65 samples/male for 8 males high Mn & 10 males low Mn



ear clip, hair, retina, skull
muscle, olfactory bulb,
neocortex, cerebellum

testes, quadriceps, triceps,
femur bone marrow

lung, heart, liver, kidney, gall bladder,
spleen, pancreas, mesenteric lymph
node, small intestine, adipose tissue

What's next for Groote Island?

Do children with higher Mn body burdens have poorer cognition and motor performance?

How does the trophic ecology of an animal determine its bioaccumulation of Mn?



ANINDILYAKWA RANGERS

THREATENED SPECIES
RECOVERY CENTRE

